UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2013-1186

SMARTGENE, INC.,

Plaintiff-Appellee,

v.

ADVANCED BIOLOGICAL LABORATORIES, SA, and ABL PATENT LICENSING TECHNOLOGIES, SARL,

Defendant-Appellant.

Appeal from the United States District Court for the District of Columbia in Case No. 08-CV-0642, Judge Beryl A. Howell

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APPELLANTS' OPENING BRIEF

Robert R. Sachs
Michael J. Sacksteder
Daniel R. Brownstone
Jeffrey V. Lasker
FENWICK & WEST LLP
555 California St., 12th Floor
San Francisco, CA 94104
Tel: (415) 875-2300
Fax: (415) 281-1350
rsachs@fenwick.com
msacksteder@fenwick.com
dbrownstone@fenwick.com
jlasker@fenwick.com

Edward W. Goldstein
GOLDSTEIN LAW, P.L.L.C.
710 N. Post Oak Rd., Suite 350
Houston, Texas 77024
Tel: (713) 877-1515
egoldstein@gliplaw.com

Attorneys for Defendants-Appellants Advanced Biological Laboratories, SA and ABL Patent Licensing Technologies, SARL

CERTIFICATE OF INTEREST

Counsel for Appellant Advanced Biological Laboratories, SA, *et al.* certifies the following:

1. The full name of every party or *amicus curiae* represented by me is:

   Advanced Biological Laboratories, SA

   ABL Patent Licensing Technologies, SARL

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

   Advanced Biological Laboratories, SA

   ABL Patent Licensing Technologies, SARL

3. All party corporations or any publicly held companies that own 10 percent or more of the stock of the party or *amicus curiae* represented by me are:

   Advanced Biological Laboratories, SA has no parent corporation and no publicly held corporation owns more than ten percent of its stock. ABL Patent Licensing Technologies, SARL is a wholly owned subsidiary of Advanced Biological Laboratories, SA.

4. The names of all the law firms and the partners or associates that appeared for the party or *amicus curiae* now represented by me in the trial court or agency or are expected to appear in this court are:

Robert R. Sachs, Michael J. Sacksteder, Daniel R. Brownstone, Jeffrey V. Lasker of Fenwick & West; Edward W. Goldstein, Alisa A. Lipski, Califf T. Cooper of Goldstein Law, PLLC; Robert H. Epstein of Epstein & Gerken

Dated: June 20, 2013

Respectfully submitted,

FENWICK & WEST LLP

/s/ Robert R. Sachs
Robert R. Sachs

Counsel for Appellants
Advanced Biological Laboratories, SA
and ABL Patent Licensing
Technologies, SARL

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STATEMENT OF RELATED CASES

Counsel for Defendants-Appellants are not aware of any other case pending in this or any court involving these parties or patents, although numerous other pending appeals involve similar questions of patent eligibility under 35 U.S.C. § 101. *See, e.g.*, *Sinclair-Allison Inc. v. Fifth Avenue Physician Servs. LLC*, No. 2013-1177; *OIP Technologies, Inc. v. Amazon.com, Inc.*, No. 2012-1696; *Digitech Information Sys. v. BMW Auto Leasing*, No. 2012-1414; *Bancorp Servs. v. Sun Life*, No. 2011-1467; *WildTangent v. Ultramercial*, No. 2011-962.

JURISDICTIONAL STATEMENT

This Court has exclusive jurisdiction under 28 U.S.C. § 1295(a)(1). The district court entered a final judgment for SmartGene, Inc. ("SG") on January 3, 2013. A39. Advanced Biological Laboratories, SA and ABL Patent Licensing Technologies, SARL (collectively, "ABL") timely filed their notice of appeal on January 28, 2013. A2893.

STATEMENT OF THE ISSUES

Whether the district court erred in holding that all claims of United States Patent Nos. 6,081,786 and 6,188,988, which disclose a computerized expert system for selecting treatment alternatives for patients with identified diseases or conditions, are ineligible subject matter under 35 U.S.C. § 101.

Whether the district court erred in refusing to reconsider its grant of summary judgment in view of *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S.Ct. 1289 (2012),

Whether the district court erred in invalidating all claims of the ABL patents based on an analysis of one claim.

Whether the district court erred in striking evidence submitted by ABL in connection with its motion for reconsideration, which was offered to support ABL's position with respect to new standards announced in *Prometheus*.

STATEMENT OF THE CASE

I. INTRODUCTION

In this declaratory patent action initiated by SmartGene ("SG"), ABL alleges infringement of claims 1 and 23 of U.S. Patent Nos. 6,081,786 (the "'786 patent") and 6,188,988 (the "'988 patent") (collectively, the "ABL patents"). These patents, which teach a method, system, and computer program for a medical expert system for identifying treatment options, have survived multiple reexamination attempts by SG, with all claims emerging unchanged. This appeal concerns the eligibility of the ABL patents' claims under 35 U.S.C. § 101.

II. THE PROCEEDINGS BELOW

SG filed this declaratory judgment action on May 8, 2008, asserting noninfringement and invalidity of the ABL patents. A61-A62. Before any significant discovery, the case was stayed pending reexamination of the ABL

patents. A248. More than two years later, the ABL patents emerged from reexamination unchanged, and the stay was lifted. *See* A282-A283; A1026; A1069. Without substantial discovery pertinent to claim scope, SG moved for summary judgment that the independent claims of the ABL patents were directed to ineligible subject matter. *See* A366. While this motion was pending, the parties submitted claim construction briefs. A660-683; A800-822; A916-939. Without ruling on claim construction, the district court granted SG's summary judgment motion, finding that all claims of both patents recited unpatentable subject matter. A38. The district court relied on the then-existing § 101 jurisprudence, including the district court opinion from *CLS Bank International v. Alice Pty. Ltd.*, 768 F. Supp. 2d 221 (D.D.C. 2011). The court also relied heavily on *Prometheus*, which had issued only ten days before its ruling, without considering the extent to which that opinion impacted the evidentiary basis for the court's decision.

ABL timely moved for reconsideration pursuant to Fed. R. Civ. P. 59(e), asserting that the district court improperly invalidated all claims of the ABL patents—even **unasserted** claims—after analyzing only a single claim, and that *Prometheus* changed § 101 law. With this motion, ABL submitted additional evidence consistent with its position that *Prometheus* announced standards for patent eligibility, particularly in regard to "conventional" and "routine" activity that required the district court to base its decision on specific facts in the record,

rather than judicial intuition and speculation. The district court refused to reconsider its summary judgment order, and ABL timely appealed.

STATEMENT OF THE FACTS

I. THE TECHNOLOGY

Virtually all doctors lack comprehensive knowledge of the state of the art in their field, as today's most complicated medical problems often require broader and deeper expertise than possessed by even the most highly-trained physicians. It has become nearly impossible for physicians to keep up with rapidly evolving techniques and treatment alternatives because cutting-edge research produces new results almost every day. A975 ¶¶ 11-13. These deficits are particularly pronounced in fields on which research institutions focus, such as immunodeficiency diseases.

Advanced information technology augments physicians' capabilities. Computerized medical expert systems can integrate information about ongoing research and provide physicians with up-to-date, state-of-the-art guidance and recommendations for treatment that they could not singlehandedly marshal.

Computerized expert systems typically assist physicians in fields where decisions involve many variables and conditions. A2650. Expert systems are one application of "artificial intelligence," a field of computer science that dates back to the early 1950s. A2648. An expert system typically contains a "knowledge

base" and an "inference engine." A92 at col. 7 ll. 45-56 & col. 8 ll. 22-25. The knowledge base is a database of rules (written in computer code) for evaluating particular "facts" (also expressed in computer form and stored in a database) in a given situation. *Id.* Rules are generally encoded in a manner similar to "If *premise*, then *conclusion*" logic. A94 at col. 11 ll. 14-34. In a medical expert system, the rules can define relationships between medical facts and medical treatments. *See* A2650. In the ABL patents, some rules define specific relationships between different types of drugs for treating HIV. An example rule is: "Rule #1: If the eval therapy contains Zidovudine (AZT) and Stavudine (d4T), then reject the therapy." A93 at col. 10 ll. 44-53. (This is an English expression of the rule, which when implemented in the expert system, is expressed in specific data structures and code instructions). The inference engine is the mechanism that applies the rules to the initial input facts, and then "chains" together the outputs of these rules as the inputs to further rules, until a final conclusion results. *Id*.

While expert systems encode expert information and simulate the type of logical reasoning that humans perform, they are nonetheless inherently computer systems and programs. The United States Patent and Trademark Office ("USPTO") has long recognized artificial intelligence systems and expert systems generally, including medical expert systems, as technology. *See* A1108-A1112. The USPTO provides a specific set of patent classifications for artificial

intelligence: Class 706, with a multiple subclasses related to specific types ("applications") of artificial intelligence and expert systems, ranging from industrial control (Class 903), power plants (Class 915), elevators (Class 918), construction (Class 923), education (Class 927), geological analysis (Class 929), and, of course, medicine (Class 924). A1099; A1113-A1114. More than 10,000 patents have issued in Class 706,[1] dating as far back as 1976. Accordingly, the USPTO has developed considerable expertise in examining patents related to artificial intelligence and expert systems.

ABL's technology, marketed as TherapyEdge, provides a specific type of expert system for the problems presented by the vast array of treatment options available to—but not necessarily known by—physicians in a given field. *See* A982-A985; A1071-A1093. Physicians use the TherapyEdge system to identify a set of treatment options for complex disorders such as cancer and HIV, for which the standard of care evolves too rapidly for individual physicians to track. *Id.* By providing physicians the benefit of more than their minds could retain (and more information than they could survey in a lifetime), ABL's technology improves patient treatment and outcomes. A976 at ¶ ¶15,16; A985; A1092.

[1] *See Patent Database Search Results*, USPTO Patent Full-Text and Image Database, http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&u=%2Fnetahtml%2FPTO%2Fsearch-adv.htm&r=0&p=1&f=S&l=50&Query=ccl%2F706%2F%24&d=PTXT (last visited June 14, 2013).

II. THE ABL PATENTS

The ABL patents disclose and claim an interactive computer expert system 20 that assists a physician in tracking and optionally ranking treatment regimens on the basis of individualized patient information. *See* A67-A68 at Figs. 1-2; A520-522. The system 20 is used in an interactive manner. The physician first inputs data concerning the patient's condition and preferred options. The system 20 evaluates those conditions and options using three knowledge bases 21, 22, 23 and an inference engine 26 for processing the rules and information therein, and outputs a ranked listing of recommendations 27. A first knowledge base 21 stores different therapeutic treatment regimens for different medical diseases or conditions. A second knowledge base 22 stores the expert rules for evaluating and selecting therapeutic treatment regimens. A third knowledge base 23 stores advisory information associated with specific constituents of the various therapeutic treatment regimens. Table 3 of the '786 Patent summarizes the various types of rules. A94 at col. 11 ll. 45-60.

The patents illustrate examples of the evaluation of therapeutic regimens. FIG. 6A illustrates a ranked list of therapy options 76. *See also* FIG. 10B (showing a ranked listing of therapy options, and an advisory warning at 73); FIG. 11C (showing ranked listing of therapy options, and an advisory warning); FIG. 12B (showing explanation of rejected therapy).

Figure 1 of each patent is a flowchart that illustrates the interactive operation of the expert system, showing steps (10, 11, 14, 16, 18) by the physician to enter data, and steps (12, 13, 15, 17) by the expert system to process the data and generate therapeutic regimens and advisory warnings:

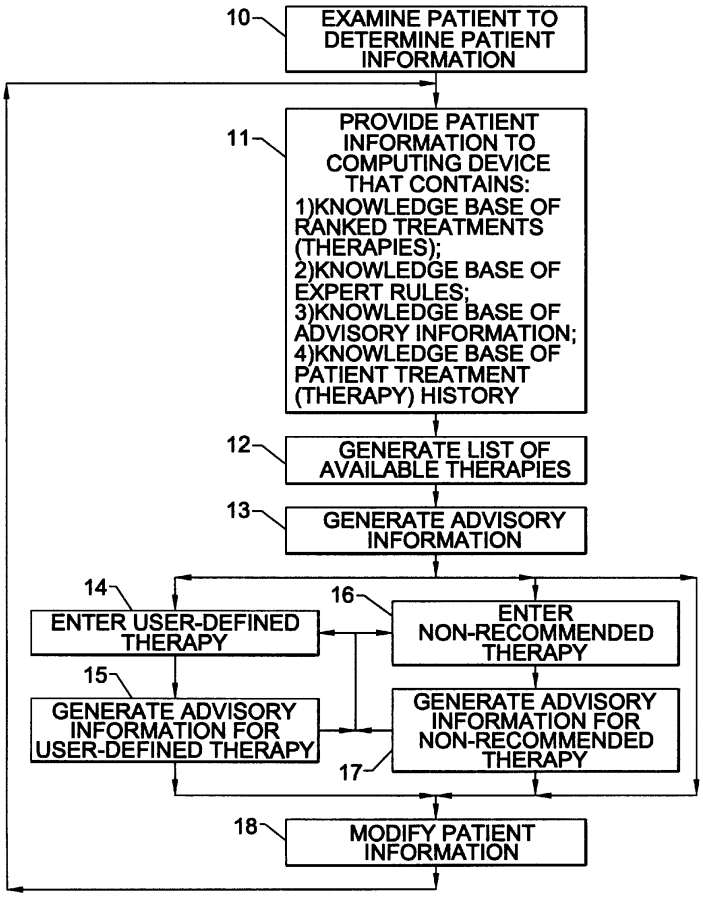

FIG. 1.

Each of the ABL patents contains three independent claims: system claims directed to an expert system computer, method claims directed to the operation of that expert system computer, and computer product claims directed to a computer

program implementation of software. *See* A97-A99 at claims 1, 23, 45. Twenty-one dependent claims depend from each independent claim and detail different features of the expert system. *Id.*

SUMMARY OF THE ARGUMENT

The claims of the ABL patents are patent-eligible under § 101 because they do not preempt all practical applications of the abstract idea of evaluating treatment options for patients with medical conditions. The claims have meaningful limitations which restrict them from covering all practical uses of the abstract idea. Claim 1 of the '786 patent and claim 1 of the '988 patent both recite a step of:

> (a) providing patient information to *a computing device comprising*:
> *a first knowledge base* comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;
> *a second knowledge base* comprising a plurality of expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition;
> *a third knowledge base* comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens;

A97 at col. 17 ll. 52-64; A132 at col. 17 l. 55–col. 18 l. 4 (emphasis added).[2]

Claim 1 of the '786 patent also recites the step of:

> (b) generating in said computing device a ranked listing of available therapeutic treatment regimens for said patient;

A97 at col. 17 ll. 65-67.

[2] Unless otherwise indicated, emphasis in quotations is added.

These limitations must be interpreted according to the knowledge of one of skill in the art—a computer scientist or engineer within the field of artificial intelligence and expert system design. To one of skill in the art, the first claim limitation recites a *physical computer*, one with three specifically defined knowledge bases. The second limitation similarly recites a specific operation of that physical computer, the generation of a ranked list of treatments.

One of skill in the art can readily "practice" the abstract idea of "evaluating, considering and constructing treatment options for a patient presenting a specific medical condition" without using the claimed computing device with its specific knowledge bases or ranking function. First, doctors can and have treated patients without using a computer at all. Second, physicians can use conventional computers that do not have the claimed knowledge bases and ranking operations. Finally, the examiner identified multiple examples of computer systems that practice the abstract idea and that do not have the claimed knowledge bases and ranking features. Thus, not only it is possible to practice the abstract idea here, but it has been and continues to be done, all outside of the scope of the ABL patent claims. Thus, the ABL patent claims do not preempt all and every practical application or commercial use of the abstract idea.

The ABL patent claims further satisfy the machine or transformation test, since they recite a particularly defined machine, a computing device with specifically defined knowledge bases.

The district court erred by not applying the proper preemption methodology. First, the court erred by reading the claims as reciting nothing more than steps performed in the human mind. A person of ordinary skill in the art, a computer scientist or engineer, would understand the claims to recite a physical computer with specific knowledge bases. Second, the court failed to unambiguously identify the abstract idea underlying the claims. Third, the court considered the claim limitations by analogizing them to the thoughts and actions of physicians, rather than considering evidence of whether the real world effect is to cover all practical applications of that abstract idea. The court concluded—without any proper *evidence*—that the claim limitations were the routine and conventional actions of doctors.

Finally, the court further erred in denying ABL's motion for reconsideration, which sought to introduce evidence demonstrating that the claim limitations were not routine and conventional.

ARGUMENT

I. STANDARD OF REVIEW

Because patent eligibility is an issue of substantive patent law, Federal Circuit law applies to the district court's grant of summary judgment. This Court reviews the district court's grant of summary judgment of patent eligibility under 35 U.S.C. § 101 *de novo*.

The D.C. Circuit reviews a district court's refusal to grant a motion for reconsideration under Fed. R. Civ. P. 59(e) *de novo* only if the district court addressed the merits of a new theory raised for the first time in the reconsideration motion. *E.g.*, *Dyson v. District of Columbia*, 710 F.3d 415, 419-20 (D.C. Cir. 2013) (reviewing *de novo*). In other words, while a decision *whether to consider* theories raised in a Rule 59(e) reconsideration is reviewed for abuse of discretion, a decision *addressing the merits* of these theories is reviewed *de novo*. *Id.*

ABL's reconsideration motion articulated new theories of patent eligibility based on *Prometheus* and on ABL's concurrently submitted evidence. In particular, ABL argued: (1) that the district court erred in invalidating all claims of both patents, including unasserted claims; (2) that the district court erred by doing this on the basis of an analysis of one claim; and (3) that the Supreme Court's *Prometheus* decision represented a change in law calling for reconsideration of the district court's earlier summary judgment opinion. A43. Importantly, the district

court considered the merits of each of these arguments. *Id.* ("The Court *addresses* these arguments *seriatim* below."). For example, the district court decided that *Prometheus* was a clarification—rather than a change—in controlling law. A53. The discussion thus squarely addressed ABL's new theory of eligibility in connection with its reconsideration motion. Therefore, under the law of the D.C. Circuit, the district court's decision not to reconsider its grant of summary judgment is also reviewed *de novo*.

II. THE DISTRICT COURT ERRED IN HOLDING THAT ABL'S PATENTS DO NOT CLAIM PATENT-ELIGIBLE SUBJECT MATTER

A. Patent Claims Are Entitled to a Presumption of Eligibility

ABL's claims are entitled to a presumption of validity. 35 U.S.C. § 282. This presumption applies to all bases for invalidity, including § 101 challenges. *CLS Bank Int'l v. Alice Corp. Pty. Ltd.*, No. 2011-1301, 2013 U.S. App. LEXIS 9493, at *40 (Fed. Cir. May 10, 2013) (en banc) (Lourie, J., concurring) (the presumption of validity "applies when § 101 is raised as a basis for invalidity"); *id.* at *100-01 (Rader, J., concurring-in-part and dissenting-in-part) ("Because we believe the presumption of validity applies to all challenges to patentability, including those under Section 101 and the exceptions thereto, we find that any attack on an issued patent based on a challenge to the eligibility of the subject matter must be proven by clear and convincing evidence."). Each of ABL's claims

is entitled to its own presumption of validity, determined claim by claim: The validity of any claim depends upon the claim's unique and full set of limitations. *See, e.g.*, *Nat'l Steel Car, Ltd. v. Canadian Pac. Ry., Ltd.*, 357 F.3d 1319, 1334 (Fed. Cir. 2004).

B. A Claim Is Patent-Eligible Unless It Preempts All Practical Applications Of An Abstract Idea.

The question of whether a claim is patent-eligible does not begin and end with a statement that the claim implicates an abstract idea, law of nature, or natural phenomenon. Rather, the question is whether the scope of the claim "wholly preempts" *all practical applications* of the abstract idea, law of nature, or natural phenomenon. The Supreme Court has consistently looked to the scope of the claim itself and compared it with the range of practical applications of the underlying abstract idea. In *Bilski*, the Supreme Court stated that "Claims 1 and 4 in petitioners' application explain the basic concept of hedging" and that "[a]llowing petitioners to patent risk hedging would pre-empt use of this approach in *all fields*, and would effectively grant a *monopoly over an abstract idea*." *Bilski v. Kappos*, 130 S. Ct. 3218, 3231 (2010). In *Benson*, the claims "purported to cover *any use* of the claimed method in a general-purpose digital computer of any type," such that "the patent would *wholly pre-empt* the mathematical formula and in practical effect would be a patent on the algorithm itself." *Gottschalk v. Benson*, 409 U.S. 63, 64, 71-72 (1972). By contrast, in *Diehr*, the claims were

patent-eligible because "they do not seek *to preempt the use* of [the Arrhenius] equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process." *Diamond v. Diehr*, 450 U.S. 175, 187 (1981).[3] In *Prometheus*, the Court emphasized that Prometheus' claims "threaten to inhibit the development of more refined treatment recommendations" because "[t]he determining" step too is set forth in highly general language *covering all processes* that make use of the correlations after measuring metabolites, including later discovered processes that measure metabolite levels in new ways." *Prometheus*, 132 S.Ct. at 1302.

This Court has clarified the importance of the preemption analysis, with its central focus on the scope of the claim relative to *all practical applications* of the abstract idea, and the important role that factual evidence plays in this analysis. "The question under § 101 reduces to an analysis of what additional features

[3] Justice Stevens, a harsh critic of computer-based inventions, looked to the claim language, not some "plain English" distillation. In *Flook*, Justice Stevens consistently focused on the claim language: "The *patent claims* cover any use of respondent's formula for updating the value of an alarm limit on any process variable involved in a process comprising the catalytic chemical conversion of hydrocarbons . . . . Our approach to respondent's application is, however, not at all inconsistent with the view that *a patent claim* must be considered as a whole." *Parker v. Flook*, 437 U.S. 584, 586, 594 (1978). In *Bilski*, Justice Stevens made clear that the focus is on the claim language. Stevens could have, *but did not*, say "A method of doing business does not qualify as a "process" under § 101." Instead he stated: "*a claim that merely describes* a method of doing business does not qualify as a "process" under § 101." *Bilski*, 130 S.Ct. at 3233 (Stevens, J., concurring).

remain in the claims" and whether the claims "impermissibly preempt[]" the underlying abstract idea. *Bancorp Servs., L.L.C. v. Sun Life Assurance Co. of Can.*, 687 F.3d 1266, 1279-80 (Fed. Cir. 2012) (internal citation omitted) (quoting *Benson*, 409 U.S. at 72). The majority of the concurring and dissenting opinions in *CLS* agree that the preemption analysis is the primary tool for determining patent eligibility. "What matters is whether a claim threatens to subsume the full scope of a fundamental concept, and when those concerns arise, we must look for meaningful limitations that prevent the claim as a whole from covering the concept's *every practical application*." *CLS*, 2013 U.S. App. LEXIS 9493, at *29 (Lourie, J., concurring). "The Supreme Court has told us that a claim is not meaningfully limited if its purported limitations provide no real direction, *cover all possible ways to achieve the provided result*, or are overly-generalized." *Id.* at *89 (Rader, J., concurring-in-part and dissenting-in-part). "Pre-emption is only a subject matter eligibility problem when a claim preempts *all practical uses* of an abstract idea." *Id.* at *87 (Rader, J., concurring-in-part and dissenting-in-part). "While it is possible these claims may have been obvious over the prior art—which, of course, would include the abstract idea itself—they do not *preempt all commercial uses or applications* of that idea." *Id.* at *176 (Linn, J., dissenting). As each of these, and many other expressions of the preemption test make clear, the

issue is not whether the claim preempts *some* application of the abstract idea, but whether it preempts "every" and "all" practical applications.[4]

The question of preemption is answered by considering whether there are "meaningful limitations." "[T]he balance of the claim can be evaluated to determine whether it contains additional substantive imitations that narrow, confine, or otherwise tie down the claim so that, in practical terms, it does not cover the full abstract idea itself." *Id.* at *33 (Lourie, J., concurring). "A claim may be premised on an abstract idea—the question for patent eligibility is whether the claim contains limitations that meaningfully tie that idea to a concrete reality or actual application of that idea." *Id.* at *85 (Rader, J., concurring-in-part and dissenting-in-part).

In considering whether a limitation is meaningful, this Court and the Supreme Court have adopted various guidelines. First, "while no particular type of limitation is necessary, meaningful limitations may include the computer being part of the solution, being integral to the performance of the method, or containing an improvement in computer technology." *Id.* at *92 (Rader, J., concurring-in-part and dissenting-in-part).

[4] "To be clear, the proper focus is not preemption per se, for some measure of preemption is intrinsic in the statutory right granted with every patent to exclude competitors." *Id.* at *28-29 (Lourie, J., concurring).

Second, a claim "will not be limited meaningfully if it contains *only* insignificant or token pre-or post-solution activity—such as identifying a relevant audience, a category of use, field of use, or technological environment." *Id.* at *88 (Rader, J., concurring-in-part and dissenting-in-part) (citing *Prometheus*, 132 S.Ct. at 1297-98, 1300-01; *Bilski*, 130 S. Ct. at 3230-31; *Diehr*, 450 U.S. at 191-92 & n.14; *Parker v. Flook*, 437 U.S. 584, 595 n.18 (1978)).

Third, limitations that are "well understood, routine, conventional activity previously engaged in by scientists who work in the field" are also not meaningful. *Prometheus*, 132 S.Ct. at 1298. In *Prometheus*, the Court found that the claims were nothing more than the "steps that must be taken in order to apply the laws in question." *Id*. at 1299. In *CLS*, the steps were simply "generic computer functionality" which "evinces little human contribution." 2013 U.S. App. LEXIS 9493, at *45-46 (Lourie, J., concurring).

Whether a claim limitation is "meaningful" is determined through the eyes of one of skill in the art, precisely because that is who would "practice" the invention by creating a "practical application" of the abstract idea. This determination is necessarily a question of fact, because it "centers on practical, *real-world* effects of the claim." *Id.* at *36 (Lourie, J., concurring). Thus, a claim cannot be found patent ineligible unless clear and convincing evidence, such as expert testimony, proves that the "practical, real world effect" of the claim it is to

cover "every practical application" of the alleged abstract idea (however that idea is defined). Importantly, a court cannot determine whether a limitation is "insignificant," "pre or post solution activity," or "conventional and routine" based on its own intuition or experience: What is meaningful to one of ordinary skill may (incorrectly) appear trivial to a lay person unfamiliar with the technology's subtleties. Further, summary judgment of patent ineligibility is inappropriate unless clear and convincing evidence proves that not a *single* limitation of the claim is "meaningful" in this manner.

Another, perhaps more convenient, formulation of the preemption test asks whether, given the presumption of validity, the patent defendant can prove by *evidence*, not argument, that *no practical implementation* of the abstract idea would avoid infringement. This is a logical corollary to establishing that the claim covers all practical applications. In short, the movant must produce evidence, such as expert testimony, that it would be impossible to avoid infringing the claim while practicing the identified abstract idea. The patentee, by contrast, need only show at the summary judgment stage a genuine issue of fact as to whether *some* way exists to avoid the patent claim and still practice the abstract idea.

C. The Abstract Intellectual Idea In A Patent Claim Is Not The Same As An Abstraction.

A necessary precursor to the analysis of "meaningful limitations" is a definition of the abstract intellectual idea the claim is purported to recite. "In

short, one cannot meaningfully evaluate whether a claim preempts an abstract idea until the idea supposedly at risk of preemption has been unambiguously identified." *CLS*, 2013 U.S. App. LEXIS 9493, at *33 (Lourie, J., concurring). This is not always a simple task, because "[a]ny claim can be stripped down, simplified, generalized, or paraphrased to remove all of its concrete limitations, until at its core, something that could be characterized as an abstract idea is revealed." *Id.* at *81 (Rader, J., concurring-in-part and dissenting-in-part). The key is to focus on whether the claim as a whole covers an abstract *intellectual* idea, as opposed to making use of the types of "abstractions" that are properly part of all patent claim drafting.

1. The Abstract Idea Analysis Properly Focuses On Abstract Intellectual Ideas.

The Supreme Court and this Court have consistently declined to define exactly what makes an idea "abstract." *See, e.g., Bilski*, 130 S.Ct. at 3236 (Stevens, J., concurring) (The Court has "never provide[d] a satisfying account of what constitutes an unpatentable abstract idea."); *MySpace, Inc. v. GraphOn Corp*., 672 F.3d 1250, 1259 (Fed. Cir. 2012) ("When it comes to explaining what is to be understood by "abstract ideas" in terms that are something less than abstract, courts have been less successful."); *Research Corp. Techs. v. Microsoft Corp*., 627 F.3d 859, 868 (Fed. Cir. 2010) ("[T]his court also will not presume to define "abstract"

beyond the recognition that this disqualifying characteristic should exhibit itself so manifestly as to override the broad statutory categories of eligible subject matter").

However, a subtle but important shift in the focus of the §101 inquiry has occurred since it was first introduced by the Supreme Court. The limitation on §101 is more precisely on abstract *intellectual* ideas, not on "abstractions" generally: "Phenomena of nature, though just discovered, mental processes, abstract *intellectual* concepts are not patentable, as they are the basic tools of scientific and technological work." *Benson*, 409 U.S. at 67. And in referring to *Benson*, the Court in *Diehr* stated: "[T]he Court clearly held that new mathematical procedures that can be conducted in old computers, like mental processes and abstract *intellectual* concepts, are not patentable processes within the meaning of §101." *Diehr*, 450 U.S. at 201 (internal citation omitted).

Over time, the use of the modifier "intellectual" has been dropped, and "concepts" has been replaced by "ideas," and now the Supreme Court and other courts simply refer to "abstract ideas." *See, e.g., Bilski* 132 S.Ct. at 3229. Even so, it is clear that the *original concern* of the Supreme Court was with "ideas" that are purely mental in nature, such as "mental processes," (*Benson, Diehr*) and "scientific truths." *See Diehr*, 405 U.S. at 201; *Benson*, 409 U.S. at 67; *Mackay Radio & Tel. Co. v. Radio Corp.*, 306 U.S. 86, 94 (1939). Indeed, the traditional definition of "idea" refers *specifically* to the mental phenomenon: "any conception

existing *in the mind* as a result of mental understanding, awareness, or activity." *Idea Definition*, Dictionary.com, http://dictionary.reference.com/browse/idea (last visited June 6, 2013); *see also* "Idea," Webster's Third New International Dictionary 1122 (2002) ("an object *of the mind* existing in apprehension, conception, or thought; a product of reflection or mental conception").

All human language—and all patent claims—make use of concepts. Thus, the proper focus of the § 101 inquiry is not on "abstract ideas" generally—but on "intellectual concepts," because these are "basic tools of scientific and technological work." *Concrete* concepts such as *computer*, *house*, *dog*, *container*, *poem*, *mammal*, *run*, *burn*, and *cook* are used to reference physical objects, actions, their attributes, and relationships. By contrast, *abstract intellectual concepts* are concepts that do not have—and could not have—distinct physical manifestation in the world. Thus, *truth*, *fairness*, *justice*, *democracy*, and *humility* are abstract *intellectual* ideas pertaining to humans and social relationships; prime numbers, irrational numbers, negative numbers are examples of purely abstract intellectual concepts in mathematics. Judge Rader articulated this distinction: "An abstract idea is one that has no reference to material objects or specific examples—i.e., it is not concrete." *CLS*, 2013 U.S. App. LEXIS 9493, at *85 (Rader, J., concurring-in-part and dissenting-in-part) (citing Merriam-Webster's Collegiate Dictionary 5 (11th ed. 2003) (defining "abstract" as "disassociated from any specific

instance . . . expressing a quality apart from an object <the word poem is concrete, poetry is [abstract]>")). In short, if "it's something you can drop on your foot," then it's not an abstract idea. John Maguire, *The Secret to Good Writing: It's About Objects, Not Ideas*, The Atlantic (October 2, 2012, 9:30 AM), http://www.theatlantic.com/national/archive/2012/10/the-secret-to-good-writing-its-about-objects-not-ideas/263113/.

However, there is a difference between an *abstract intellectual idea* and an *abstraction*, and this difference is overlooked in many discussions of patent eligibility. An *abstraction* is a generalization – a term or definition that identifies the principal aspects or features of the concept that are relevant to a given context, while removing features that are not important: "the act or process of leaving out of consideration one or more qualities of a complex object so as to attend others." "Abstraction," Webster's Third New International Dictionary 8 (2002).

One use of abstraction is classification. Some concepts reference a particular *species*, and some concepts reference the *genus*—the genus may be considered an *abstraction* of the species. The concept of a *container* is an *abstraction* over various species such as *cup*, *glass*, *tumbler*, *stein*, *pitcher*, *champagne flute.* What makes *container* an abstraction is that it connotes the features that are common to these objects—e.g., generally hollow, capable of holding some substance—while eliminating the particulars that differentiate

them—size, shape, attributes such as handles, and the materials they are intended to contain. But a *container* is clearly not an abstract *intellectual* idea—you can "drop it on your foot" —unlike *humility* or *democracy*. There are many examples of what could be called *concrete abstractions*: *mammal*, *vehicle*, *communication device, telephone,* and *publication*. Similarly, there can be abstractions pertaining to abstract intellectual ideas. *Virtue* is an abstraction of different species such as *humility*, *integrity*, *courage*, etc. *Government* is abstraction covering *democracy*, *oligarchy*, *republic*, *monarchy*, etc.

Clearly then, the abstraction of a *container* could contribute to eligible subject matter, while the abstraction of *government* could not. Thus, labeling a claim as an *abstraction* **does not in any way** answer the question as to whether the claim is for an *abstract intellectual* concept or a concrete concept. This distinction between *abstract intellectual ideas* and *abstractions* makes all the difference "in the real world" of patent claims.

2. The ABL Patent Claims Make Proper Use Of Abstractions, Not Abstract Ideas.

By design and practice, patent claims necessarily make use of *abstractions*. This has been long recognized:

> The difficulty which American courts . . . have had . . . goes back to the primitive thought that an "invention" upon which the patent gives protection is something tangible. The physical embodiment or disclosure, which, in itself is something tangible is confused with the definition or claim to the inventive novelty, and this definition or

> claim or monopoly, also sometimes called "invention" in one of that word's meanings is not something tangible, but is an abstraction. *Definitions are always abstractions*. This primitive confusion of "invention" in the sense of physical embodiment with "invention" in the sense of definition of the patentable amount of novelty, survives to the present day, not only in the courts, but among some of the examiners in the Patent Office.

Emerson Stringham, *Double Patenting* 209 (1933).

As the *Phillips* en banc court stated, "persons of ordinary skill in the art rarely would confine their *definitions of terms* to the exact representations depicted in the embodiments." *Phillips v. AWH Corp*., 415 F.3d 1303, 1323 (Fed. Cir. 2005) (en banc). The only way those of skill in the art do not "confine their definition" to an exact representation is by the use of abstractions, so that claims are not limited to the disclosed embodiments.

The process of claim drafting by abstracting more general nouns and verbs from specific ones is not some artifice or exercise in "clever drafting" by patent attorneys, any more than the use of careful definitions in contracts amounts to clever drafting by contract lawyers. Rather, it is the fundamental way in which claims are written. Contract attorneys use particular clauses for granting a license or making an offer. So too, patent attorneys select particular terms, whether narrow or broad, as necessary to distinguish the claim over the prior art. "The choice of which word (gerund) to use for introducing a method step is similar to the choice of which word to use for describing elements in apparatus claims.

Generally, one chooses the broadest word the prior art will allow." Robert C. Faber, *Landis on Mechanics of Claim Drafting* 102 (3d Ed. 1990). Indeed, the parallel between contract drafting and claim drafting is particularly *apropos* because patent claims form the essential part of the bargain between the grant of the patent right in exchange for the disclosure of the invention.

In view of the foregoing, there is a difference between a *broad* process claim that uses various *abstractions* and a claim that itself covers an *abstract intellectual idea*. The former can exist without the latter. A broad claim is acceptable, and may be patent-eligible and patentable (novel and non-obvious), as long as it is definite and supported by the disclosure. Thus, the proper analysis is whether the subject matter of the claim *as a whole* is directed to *abstract intellectual ideas*, not whether the claim makes use of abstractions, which every claim must do.

The ABL patent claims make proper use of abstractions. The recitations of a "computing device" and "knowledge bases, "generating" and "ranked listing" are abstractions in the field of computer science, not abstract intellectual ideas. A "computing device" is a generalization for different specific computers that may be used to implement the invention. A "knowledge base" is a generalization used in the expert system field to reference particular types of databases. A "ranked listing" is a description of a specific type of output produced by the computing device. Taken together, as they must be, these claim limitations recite meaningful

limitations, and articulate a particular special purpose computer for purposes of the machine or transformation test. A "machine ceases to be a general purpose computer when it is running the software. It does not, however, by virtue of the software it is running, become an abstract idea." *See CLS*, 2013 U.S. App. LEXIS 9493 at *140 (Moore, J., dissenting-in-part).

D. The ABL Patent Claims are Patent-Eligible Under The Preemption Analysis.

1. The Claims Do Not Wholly Preempt All Practical Applications of the Abstract Idea(s) The District Court Identified.

The claims of the ABL patents are patent-eligible because they do not wholly preempt all practical applications of an abstract idea. The first step in the preemption analysis is to define the abstract (intellectual) idea implicated in the claim. As discussed below in Section II.E, the district court committed several errors when it performed its patent eligibility analysis and failed to provide an unambiguous identification of the purported abstract idea. For the purposes of the instant discussion, however, ABL accepts the district court's apparent formulations, without conceding their correctness.

At best, the district court may have used the following statement as the "abstract idea" of the ABL patent claims: "evaluating, considering and constructing treatment options for a patient presenting a specific medical condition." A23. Alternatively, the court may have implicitly relied upon SG's

Local Civil Rule 7(h) Statement of Undisputed Material Facts, that the patents claim "guiding the selection of a therapeutic treatment regimen for a patient with a chronic disease or medical condition." A368.[5]

Assuming that these statements define an "abstract intellectual concept," the preemption analysis asks: do the claims of the ABL patents "wholly preempt" one from "evaluating, considering and constructing treatment options for a patient presenting a specific medical condition"? A23. Or alternatively, do they wholly preempt one from "guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition"? A97 at col. 17 ll. 49-51. The question is therefore whether are any limitations in the claims narrow the claims from "covering the concept's every practical application," *CLS*, 2013 U.S. App. LEXIS 9493, at *29 (Lourie, J.,), or "*all commercial uses or applications* of that idea" (the processing of evaluation, consideration and construction of such regimens), *id.* at *176 (Linn, J., concurring-in-part and dissenting-in-part), or "*cover[ing] all possible ways to achieve the provided result*" (the selection of a treatment regimen), *id.* at *89 (Rader, J., concurring-in-part and dissenting-in-part). Those equivalent questions are properly answered in the negative. The claims' requirement for a "computing device" comprising three distinct "knowledge

[5] That it is unclear which statement the district court used indicates that the court did not "unambiguously" define the abstract idea. *See* Section II.G below.

base[s]," each of which comprises a distinct form of information to be used for a distinct purpose, more than satisfies the requirement for "meaningful limitations" on preemption of the purported abstract idea.

a. One of Skill in the Art Would Understand The ABL Patent Claims To Be Directed Toward Computerized Expert Systems.

To decide whether the computing device limitation is "meaningful," it should be interpreted as understood by one of skill in the art, not by lay persons or the hypothetical physician that the district court seems to have employed. *See, e.g.*, *In re Suitco Surface, Inc.*, 603 F.3d 1255, 1260 (Fed. Cir. 2010) ("claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art") (internal citation omitted). This is particularly the case where the technology is complex. "Although not required, conducting a claim construction analysis before addressing § 101 may be especially helpful in this regard by facilitating a *full understanding of what each claim entails*." *CLS*, 2013 U.S. App. LEXIS 9493, at *33 (Lourie, J., concurring) (citing *Bancorp*, 687 F.3d at 1273–74). The underlying rationale is that patent eligibility rests on the full scope of the claim as understood by one of skill in the art because that is the person who would practice the claim in the real world by building practical application of the idea. A district court cannot conduct an analysis of whether the claim preempts all practical applications if it does not determine the full scope of the claim, and it

cannot determine the full scope of the claim without evidence of how those of skill in the art would understand particular limitations. Nor should the court decide on its own whether a limitation is meaningful, if there is no evidence of which alternative technologies can be used to practice the abstract idea.

There is no question that the ABL technology is extremely sophisticated: It employs artificial intelligence in general, including computer-based expert systems, and medical expert systems in particular. If the district court had determined who would be a person of ordinary skill at all, it should have identified a computer scientist with specific training and experience in artificial intelligence and expert system design, as well as medical knowledge in terms of treatment protocols for particular medical conditions.

The USPTO's classification of the patents supports such a conclusion. Courts give deference to the USPTO's expertise in classification. *See, e.g.*, *Zobmondo Entertainment, LLC v. Falls Media, LLC*, 602 F.3d 1108, 1121 (9th Cir. 2010) ("Deference to the PTO's [trademark] classification decision is sensible because the PTO has special expertise that we lack on this fact-intensive issue") (internal quotations omitted). In turn, that classification provides guidance in determining the proper person of ordinary skill in the art, which in turn influences a proper understanding of the scope of the claim. *See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 447 (Fed. Cir. 1983) ("[T]he

examiner, who with the deference we owe governmental officials we assume has some expertise in interpreting the references and some familiarity with the level of skill in the art . . . ."). In this case, the USPTO assigned the ABL patents to U.S. Class 706, relating to "Data Processing, Artificial Intelligence," and subclass 924, "Subject matter wherein the expert system provides medical related data." In the absence of any evidence or suggestion to the contrary, the USPTO's conclusion classification is both accurate and compelling evidence of the relevant field of skill in the art.

The district court made no claim to possess any skill in these fields and made no express attempt to identify the relevant field of art or the level of ordinary skill in it. Instead, to the extent it did anything in this regard, the district court examined the patents through the eyes of a hypothetical physician – a person skilled *in the wrong art*. Doctors are not trained in the computer science knowledge necessary to build ("practice") a medical expert system.[6] Again, the USPTO's classification is instructive: If a physician were a person of ordinary skill in the art of the claimed subject matter, the USPTO would have classified the invention in another class relevant to physicians, such as Class 128 ("This class includes methods of treatment of the living body and apparatus used in the

[6] In *Prometheus*, by contrast, the "relevant audience" of the claims were physicians themselves, since the claims there recited specific medical procedures. 132 S.Ct. at 1299.

inspection and treatment of diseases, wounds, and other abnormal conditions of the bodies of humans and lower animals."). The USPTO did not do so. In the absence of any specific expert testimony as to the person of ordinary skill in the art, the examiner's classification of the patent is the best evidence thereof.

b. The Claims Recite a Physical Computing Device, Not a Human Mind

The intrinsic record undermines SG's assertion and the district court's conclusion that the claimed "computing device" could encompass the human mind. First, the format of claim language is instructive. The knowledge base elements are part of step (a) and are subsumed (indented) under the "computing device" element, making these elements syntactically part of the "computing device," rather than standalone elements.

Second, the specification of the each patent discloses: "The system 20 comprises a knowledge base of treatment regimens 21, which may be ranked for efficacy (e.g., by a panel of experts) or ranked according to system rules, a knowledge base of expert rules 22, a knowledge base of advisory information 23, a knowledge base of patient therapy history 24 and patient information 25. Patient information is preferably stored within a database and is configured to be updated." A92 at col. 8 ll. 6-13; A127 at col. 8 ll. 12-19. The system 20 is described and illustrated as various physical computers (*e.g.*, central server 32, local server 34, local client 35). The central server 32 provides for central storage of the various

knowledge bases: "The central server 32 includes a central database 38, such as the Microsoft™ SQL Server application program, version 6.5 (available from Microsoft, Inc., Redmond, Wash.), executing thereon. The central server 32 ensures that the local servers 34 are running the most recent version of a knowledge base. The central server 32 also stores all patient data and performs various administrative functions including adding and deleting local servers and users to the system (20, FIG. 2)." A93 at col. 9. The local servers 34 also have copies of the knowledge bases: "Each local server 34 includes a server application, an inference engine, one or more knowledge bases, and a local database 39." *Id.*

In short, all the method claims and all of the system claims in suit recite a "computing device" which *comprises specifically defined knowledge bases*, including a knowledge base of "expert rules." The person of ordinary skill—again a computer scientist or engineer—would recognize the claim as describing a *physical computer* configured in a particular manner with particular knowledge bases for a particular type of artificial intelligence technology, an expert computer system—not a human mind with knowledge of medical treatments. Thus reading the "computing device" as a human mind, somehow disembodied from the claimed knowledge bases, ignores the evidence of the patent specification, claim language, practical reality of how computer systems operate, how the examiner classified the

patent claims, and how the examiner himself interpreted the claims (see, Section II.G below).

This analysis holds for both the system and method claims, since both claims 1 and 23 of the '786 patent recite the same computing device limitation. In *Bancorp* for example, this Court concluded that the system claims at issue required a computer, and specifically noted the description and illustration of computer in the patent specification. *See* 687 F.3d at 1274. Further, the independent method claim in *Bancorp did not* recite a computer at all, a limitation that was present only in a dependent claim. *Id.* at 1275. Here, the plain language of the method claims recites a specifically configured computing device—it cannot be "read out" of the claims as a matter of convenience.

c. The ABL Patent Claims Recite Meaningful Limitations.

The next step is to evaluate whether the ABL patents recite limitations that prevent the claim from covering "all practical applications" of the underlying abstract idea. *CLS*, 2013 U.S. App. LEXIS 9493, at *86 (Rader, J., concurring-in-part and dissenting-in-part).

The computing device limitation is one such meaningful limitation. It is incontestable that doctors evaluate, consider, construct and select treatment options for a patient presenting a specific medical condition without using a computing device at all, let alone one having specifically the claimed knowledge bases. That

is, doctors routinely "practice" the abstract idea of "evaluating, considering and constructing treatment options for a patient presenting a specific medical condition" without infringing the ABL patents. This alone demonstrates that the limitation is "meaningful," and therefore the claims are patent-eligible.

Further, there is **no evidence in the record** that these claimed knowledge bases, as implemented on computer, are necessary or inherent in any conventional computer systems that may be used by physicians in their everyday practice of evaluating patients and constructing treatment options for specific medical conditions.[7] "Instead, the question is whether these steps are inherent in an escrow. This record contains no clear and convincing evidence to that effect." *See CLS*, 2013 U.S. App. LEXIS 9493, at *105 (Rader, J., concurring-in-part and dissenting-in-part).

As noted above, the preemption analysis can be formulated as a question of the boundaries of infringement: is there *some* way to practice the abstract idea without infringing the ABL claims? The above discussion demonstrates that it is possible to create a computer-based "practical application" of the idea related to the ABL patent claims without using a computing device with the specifically claimed knowledge bases.

[7] For example, physicians typically use computer-based electronic medical records (EMR) to track patient visits and diagnoses. These EMR systems do not inherently require the use of expert systems with knowledge bases as claimed.

Not only is this possible, but it *clearly has been done*. In the file history of the '988 patent, the examiner gave a detailed statement of his reasons for allowing the claims.[8] He stated, "The specific allowable features not disclosed in the prior art are *the use of the three distinct knowledge bases recited in this claim* in combination with the listing of available treatment regimens and advisory information." A1220. The prior art of record, U.S. Patent No. 5,517,405 "Expert System for Providing Interactive Assistance in Solving Problems in Healthcare Management," disclosed "a computer-based decision support tool…[that] can be used to recommend whether or not to accept a proposed treatment for a given medical condition." *Id.* at col. 2 ll. 36-41. The '405 patent further states "The present invention provides an "expert" computer system for use in assessing proposed solutions to problems. The invention is particularly well suited to the comprehensive management of the health care of individual patients." *Id.* at col. 5

[8] Even though certain portions of the file histories of the patents-in-suit were made part of the record only in connection with ABL's motion for reconsideration, this Court may take judicial notice of the file histories of issued US patents, which are public administrative records not subject to reasonable dispute. Fed. R. Evid. 201 ("The court may judicially notice a fact that is not subject to reasonable dispute because it: . . . (2) can be accurately and readily determined from sources whose accuracy cannot reasonably be questioned"); *see, e.g., B.V.D. Licensing Corp. v. Body Action Design, Inc.*, 846 F.2d 727, 728 (Fed. Cir. 1988) (court may take judicial notice for the first time on appeal); *Eakin Enters., Inc. v. Specialty Sales LLC*, 1:11-CV-02008-LJO-SKO, 2012 U.S. Dist. LEXIS 88385, at *9-10 (E.D. Cal. June 25, 2012) (granting request to take judicial notice of patent application's full file history).

ll. 50-53. Clearly, this expert system practiced the abstract idea of "evaluating patients and constructing treatment options for specific medical conditions," **without** using the specifically claimed knowledge bases. Thus, the examiner's statement is a finding that there existed medical expert systems that practiced the abstract idea here, and that did *not* include the three claimed knowledge bases. *Id.*

No evidence in the record rebuts this finding of fact by the examiner. The point of this detailed analysis of the file history is *not* to show the novelty or non-obviousness of the claims. Rather, the examiner's analysis of the references and his express findings demonstrate there in fact existed "practical applications" of the abstract idea that did not have the computing device limitation. It *logically* follows that the claims do not "wholly preempt" the abstract idea of "evaluating, considering and constructing treatment options for a patient presenting a specific medical condition" (assuming that that this is the correct abstract idea).[9]

In *Prometheus*, the Court found that "Anyone who wants to make use of these laws **must** first administer a thiopurine drug and measure the resulting metabolite concentrations." *Prometheus*, 132 S.Ct. at 1298. There is no evidence in the record here that "anyone who wants to make use of" the abstract idea of

[9] The Examiner's findings, while made specifically in regards to the '988 patent, are equally applicable to the '768 patent, which had the same claim limitations, the same prior art references, and the very same patent Examiner. *See generally* A65-99.

"evaluating, considering and constructing treatment options for a patient presenting a specific medical condition" **must** use an expert system to begin with, let alone one configured to incorporate the specifically claimed three knowledge bases. Indeed, common sense, logic, and the record support precisely the opposite conclusion. As such, the computing device with three knowledge bases is a "meaningful limitation."

The second meaningful limitation is the "ranking" limitation. Claim 1 of the '786 patent recites "generating in said computing device a *ranked* listing of available therapeutic treatment regimens for said patient." A97 at col. 17 ll. 65-67 Claim 23 of the '786 patent recites "means for generating in said computing device a *ranked* listing of therapeutic treatment regimens for said patient." A98 at col. 19 ll. 39-41. Assuming *arguendo* that the computing device limitation did not constitute a "meaningful limitation," the requirement for the claimed systems to provide a "ranked listing" of treatment regimens provides an additional such limitation.

Although physicians admittedly may use databases in their practices, a computer database of medical information is simply a repository of data, perhaps one that can be searched based on keywords or other criteria, such as a name of disease, symptom, or drug. The results of such a search could be a list of treatments that are associated with the disease, symptom, or drug, but it would

remain the physician's task to analyze these results and decide for herself how to treat her patients. There is no evidence in the record that computer systems used by physicians *necessarily* and *inherently* "rank" treatment options.

The file history of the '786 patent supports this conclusion. In the examiner's reasons for allowance of claim 1, the examiner stated

> the *prior art of record taken either individually or in combination fails to teach* or suggest a method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition including *generating in a computing device a ranked listing of available therapeutic treatment regimens* and advisory information for one or more therapeutic treatment regimens in the ranked listing based on patient information and expert rules. The specific allowable feature, which distinguishes the present invention over the prior art is the generation of a **ranked** listing of available therapeutic treatment regimens for the patient.

A1192.

Again, the point is not to argue novelty or non-obviousness, but to highlight evidence in the record shows that "practical" medical expert systems existed that did not produce "ranked listings." Because it is possible to provide an expert system that does not include the ranking limitation, the claims do not "wholly preempt" all "practical applications" of any abstract intellectual idea.

Finally, the record contains no evidence that one of skill in the art could not have used alternative technologies to practice the abstract idea. More specifically, the claims here are for an **expert system**-type approach, as they require a knowledge base of "expert rules." There is no evidence in the record that one of

skill in the art of artificial intelligence would have to use an expert system approach at all to design a computer-based system that practices the abstract idea of evaluating and selecting treatment regimens for specific medical conditions. For example, SG provided no evidence that a medical decision support system could not have been constructed using case-based reasoning, decision trees, neural networks, or any of the many other techniques available to practitioners in the field.

In sum, the ABL patent claims do not preempt all practical or commercial applications of an abstract intellectual idea. Doctors and physicians can and will continue to evaluate and treat their patients; scientists and researchers can and will continue to identify causes and treatments of diseases, and many will do so without practicing any claim of the ABL patents. The ABL patents do not cover "basic tools of scientific and technological work." Instead, they cover a specifically defined computerized medical expert system. As such, they recite patent-eligible subject matter.

E. The District Court Failed to Correctly Apply Preemption Analysis

The district court's analysis of patent eligibility completely failed to apply the preemption analysis set forth by the Supreme Court and by this Court. Indeed, apart from quoting from the Supreme Court's cases, the district court mentioned the purported preemption effect of the claims in a single conclusory statement at

the end of the opinion, "The defendants' claims are 'invalid as being directed to an abstract idea preemptive of a fundamental concept or idea that would foreclose innovation in this area.'" A37 (quoting *DealerTrack, Inc. v. Huber*, 674 F.3d 1315, 1333 (Fed. Cir. 2012)). This is insufficient. Moreover, in addition to failing to apply preemption analysis *at all*, the district court also omitted other analytical steps that should have been included in the non-existent preemption review.

1. The District Court Failed to Interpret the Claims As Understood by Those of Ordinary Skill in the Art

Given that the preemption question always centers on the *scope of the claim*, the district court first erred by not interpreting the claim—specifically the "computing device" limitation—as understood by one of skill in the art.

The district court's mention of claim construction at the end of its opinion makes it clear that it did not properly construe the limitation in question. The court noted that ABL disputed SG's narrow construction of each of the three knowledge bases, but did not itself construe this term. A35-36. Importantly, the court did not understand the claim element of the three knowledge bases to be part of the claim element for the "computing device," thus forming a single claim limitation. A26-27. In its discussion of the "machine or transformation," the court separated the "computing device" aspect of the limitation from the three "knowledge base" features: "While the claims reference a 'computing device,' these references are insufficient to satisfy the machine test." A26. The court ignored both the claim

language itself (which indents the knowledge bases within the scope of the computing device), and for example, Fig. 1 of the '786 patent, which specifically describes a "computing device that contains: [three knowledge bases]." A67 at Fig. 1.

The district court's fundamental assumption is that the "computing device" of the claim reads on the human mind. SG specifically asserted this construction of the term in its summary judgment brief: "The treating physician's mind is the computing device." A366. The district court explicitly adopted this interpretation of the claim, in stating that "[t]he patents-in-dispute do no more than describe just such an abstract mental process engaged in routinely, either entirely within a physician's mind, or potentially aided by other resources in the treatment of patients." A19-20. This primary assumption was the start—and essentially the end—of the court's analysis, as it directly influenced every finding of the court. However, there was no *evidence* in the record that one of ordinary skill in the art would interpret the "computing device" limitation in that manner. Just as one of skill in the art of chemical engineering would not interpret a claim element for a "vat containing hydrochloric acid" as reading on the human stomach, one of skill in the art of artificial intelligence would not interpret a claim element for a "computing device" as reading on the human brain (let alone the even more

intangible "human mind"). As such, the district court's interpretation was error, and this error infected its entire analysis.

The district court's interpretation is also wholly at odds with the file histories of the patents in suit. The USPTO is required to give claim limitations their "broadest reasonable interpretation" during prosecution. *Phillips* (internal citation omitted). Nonetheless, the examiner **never** interpreted the claim limitation of the "computing device" and "knowledge bases" as reading on a human mind, but consistently interpreted it as a *physical computer with specific knowledge bases*, and thus cited as prior art other expert computer systems. *See, e.g.*, A1162 (citing the computer system disclosed in Fig. 1 of U.S. Pat. No. 5,517,405 as corresponding to the claimed "computing device . . . comprising a knowledge base"). This further demonstrates that the district court's interpretation is neither "reasonable" nor "as it would be interpreted by one of ordinary skill in the art."[10]

2. The District Court Failed to Unambiguously Define the Abstract Idea Implicated in the Claims

The district court's next error was its failure to specifically and unambiguously articulate the purported abstract idea implicated in the claim. "[I]n short, one cannot meaningfully evaluate whether a claim preempts an abstract idea

[10] The USPTO Examiner's determination of the scope of the claim is given deference. *In re Morris*, 127 F.3d 1048, 1055 (Fed.Cir.1997) (affirming the Examiner's interpretation of claims as "reasonable").

until the idea supposedly at risk of preemption has been unambiguously identified." *CLS*, 2013 U.S. App. LEXIS 9493, at *33 (Lourie, J., concurring). A careful reading of the district court's opinion shows that the court never specifically and unambiguously defined the abstract idea.

In Section III.B.6 of its opinion on summary judgment, the district court set forth a conclusory statement that "[t]he patents-in-dispute do no more than describe just such an abstract mental process engaged in routinely, either entirely within a physician's mind, or potentially aided by other resources in the treatment of patients." A19-20. That is not a definition of an abstract idea. The court then proceeded to compare the claims generally to those in *Flook*, *Diehr*, *Prometheus*, and *In re Meyer*, 688 F.2d 789 (C.C.P.A. 1982), but again without *identifying* the abstract idea.

In III.B.6.a., the court considered each step of claim 1 of the '786 patent and analogized it to the thinking or behavior of a doctor. Then in III.B.6.b., the district court ostensibly considered claim 1 "as whole," but this was no more than a summary of the previous section. The district court merely reiterated that "[i]n essence, these four steps describe abstract ideas that are commonly performed by medical professionals in evaluating, considering and constructing treatment options for a patient presenting a specific medical condition." A23. Finally, in III.C., the district court applied the "machine or transformation" test, but again without

defining any abstract idea. A23-32. If the district court did indeed rely on SG's Local Civil Rule 7(h) Statement of Undisputed Material Facts, it gave no express statement that it was doing so.

This failure to set forth a specific, unambiguous statement of the abstract idea is fatal, since in the absence of such a definition, there is nothing against which the scope of the claim at issue can be compared to determine whether it "wholly preempts" all practical application thereof.

3. The District Court Erred When It Analyzed the Claims by Analogy to a Physician's Mind

After deciding without proper expert evidence that the claimed "computing device" is either the "physician's mind" or analogous thereto, and without providing any specific definition of the abstract idea implicated by the claims, the district court improperly analogized the claim steps to those performed by a physician, arriving at the essentially foregone conclusion that all of the claimed steps and elements are merely mental steps.

Beginning with the preamble of claim 1 (which the court mistakenly labels as a "step"),[11] the court states that "this process is one that is performed in doctors' offices everyday." A22. This holding is not supported by any proper evidence in

[11] *See Pitney Bowes, Inc. v. Hewlett-Packard Co*., 182 F.3d 1298, 1305 (Fed. Cir. 1999) (preamble limiting if it is "necessary to give life, meaning, and vitality to the claim") (internal citation omitted). The district court here made no such findings.

the record. Instead, it directly adopted the statement of SG's counsel at oral argument:

> In fact about it, I was at the doctor the other day with my son, and the doctor asked my son what his issues are. He presents his issues. The doctor then tells us various steps that he could take to help him . . . So even that sort of routine encounter with the doctor implicates the claim in this case.

A2766-2767. *See* A22 ("The doctor recalls or looks up possible treatment regimens, and then advises the patient about the treatment regimen options, and the doctor's recommendation for the patient."). Thus, instead of relying on *actual evidence* of the scope of the claim as understood by one of skill in the art, the court relied on the personal experience of plaintiff's counsel, and perhaps its own knowledge. This is clearly error. *See Mintz v. Dietz & Watson, Inc*., 679 F. 3d 1372, 1377 (Fed. Cir. 2012) ("The district court made a clear error, however, in its unsubstantiated reliance on "a common sense view" or "common sense approach" to hold that it would have been "obvious to try" a locking engagement.").

For the first step of claim 1 of each of the patents-in-suit, "providing patient information to a computing device comprising [three knowledge bases]," the district court stated that "[t]he Court sees nothing in this step that is any different than the process a doctor goes through in real time when a doctor evaluates a patient." A22. Most tellingly, the court likened a significant limitation of the claim—the specific recitation of three knowledge bases—to the physician's mind,

instead of considering the *actual scope* of the limitation: "the patents' reference to three databases also *mimics* the evaluative process involved in the treatment of patients." *Id.* The court proceeded to analogize the claim element to what a doctor does:

> Specifically, after collecting patient information, a doctor would consider "therapeutic treatment regimens for said disease or medical condition" (as in the first knowledge base), consult "expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition" (as in the second knowledge base), and review "advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens" (as in the third database). The claim itself does not add anything to the process that doctors regularly engage in mentally when evaluating and treating patients.

Id.

The preemption question is not answered by analogizing claim limitations to something familiar and easy to understand. The question is answered by the scope of the claim limitations themselves. Here, the district court failed to appreciate that limitations of the three knowledge bases are part of the limitation of the "computing device," as clearly seen in the structure of the claim: "a computing device comprising: a first knowledge base . . . a second knowledge base . . . a third knowledge base." *E.g.*, A97 at col. 17 ll. 52-64. As demonstrated above, properly considered by one of skill in the art of expert systems, these limitations characterize the computing device in a specific limited fashion as a particular expert system.

The court's treatment of step (b) is even more transparently based on its own intuitions, rather than evidence in the record:

> The next step of Claim 1 of the '786 patent is "(b) generating in said computing device a ranked listing of available therapeutic treatment regimens for said patient." The Court views this step as describing what goes on in the mind of a doctor in evaluating and ranking possible treatment options for a patient based upon the benefits and counter-indicators of each option.

A22. The court's treatment of step (c) is similar: "The Court understands this step as corresponding to a doctor generating a treatment plan for a patient." A23.

Nevertheless, *no evidence* appears in the record as to what "goes on in the mind of a doctor" when evaluating treatment options; nor is that the proper object of judicial notice. There is no evidence found in the record to suggest that doctors rank "treatment options based upon the benefits and counter-indicators of each option." The only "evidence" on which the court could have reached this conclusion is its *own* intuition and experience. As such, the court erred.

F. The District Court's Application of *Prometheus* Failed to Consider Evidence of What was Routine and Conventional in the Field

Prometheus, decided eleven days after the summary judgment proceedings were completed in the district court, changed the standard in § 101 law, allowing for consideration of whether patents claims merely recite "routine" and "conventional" activity that preempts an abstract idea or law of nature. *Prometheus,* 132 S. Ct. at 1298 (holding it proper to determine patentability based

upon whether the claimed process is comprised of "well-understood, routine, conventional activity already engaged in by the scientific community"). The Supreme Court had not previously employed this approach, and had in fact rejected it. *See Diehr*, 450 U.S. at 188 (finding it improper to determine patentability under § 101 based upon whether one or more steps of the process or even the whole process, were already known or conventional). After *Prometheus*, evidence of whether claim limitations were "conventional" or "routine" became relevant to the § 101 inquiry.

Relying on *Prometheus*, the district court assumed that the steps recited in the claims at issue were "commonly performed" and consisted of "well-understood, routine, conventional activity already engaged in by the scientific community." *See* A23 (quoting the language from *Prometheus*). To the extent that the district court's analysis can be read as finding any of the claim limitations "conventional," there is no evidence in the record, beyond the court's personal intuition and experience, on which to base that conclusion.

To demonstrate that the court's assumptions were incorrect, ABL submitted with its motion for reconsideration evidence specifically showing that the claims did not recite routine and conventional activity. A955-956. The district court improperly denied ABL's motion for reconsideration and improperly granted SG's motion to strike the precise evidence submitted by ABL that *Prometheus* made

relevant for the very first time. A40-56. That decision was error. *Firestone v. Firestone*, 76 F.3d 1205, 1208 (D.C. Cir. 1996) (motion to reconsider should be granted where there is "an intervening change of controlling law, the availability of new evidence, or the need to correct a clear error or prevent manifest injustice.").

Similarly in demanding *evidence* in determining patentability, *CLS* requires consideration of evidence of the "real world" effects of the claim on "practical applications." 2013 U.S. App. LEXIS 9493, at *38 (Lourie, J., concurring). This necessarily entails a factual record, and in that context, evidence of what is "conventional and routine" is precisely the kind of evidence that goes to whether the claims cover all practical applications.

G. The District Court Erred in Holding that the ABL Patent Claims Do Not Satisfy the Machine or Transformation Test

The district court also incorrectly applied the "machine-or-transformation" test. The district court found that "[w]hile the claims reference a 'computing device,' these references are insufficient to satisfy" the machine prong for two reasons. A23. First, the court believed that the "patents-in-dispute include no special programming code, nor provide any specific algorithms that the computers would use to perform the database matching or synthesis of expert rules, advisory information, treatment regimens, and patient information." A26-27. This is error because there is no requirement that a patent specification disclose program code in order to constitute a disclosure of a particular machine. *Finisar Corp. v.*

DirecTV Group, Inc., 523 F.3d 1323, 1340-41 (Fed. Cir. 2008) ("minimal disclosure" of the programmatic detail of computer-implemented methods, allowing a "a patentee to express [the] algorithm in any understandable terms including as a mathematical formula, in prose, or as a flow chart, or in any other manner that provides sufficient structure."). Further, this Court has held that flowcharts (such as Figure 1 of the ABL patent) clearly do disclose algorithms. *E.g.*, *WMS Gaming, Inc. v. International Game Technology*, 184 F.3d 1339, 1348-1349 (Fed. Cir. 1999). "[T]he sufficiency of the disclosure of algorithmic structure must be judged in light of what one of ordinary skill in the art would understand the disclosure to impart." *Aristocrat Techs. Australia Pty Ltd. v. Int'l Game Tech.*, 521 F.3d 1328, 1337 (Fed. Cir. 2008). This is precisely the case here, where the district court failed to appreciate that an algorithmic implementation is an inherent attribute of the disclosed inference engine of Figure 1, as one of skill in the art would have recognized. There is no evidence in the record that one of skill in the art would not consider the ABL patents' specification generally, or Figure 1 specifically, as disclosing algorithms.

Second, the court held that the claims merely "reference a general purpose computer" which does not satisfy the machine prong. But again, reading the "computing device" apart from its specifically claimed knowledge bases is error, and contradicts how one of skill in the art would understand the claims. Just as one

cannot separate the "butter" from the "milk" in "buttermilk," one cannot separate the "computing device" from its "knowledge bases," as they are inherently tied together to form a single thing. And being tied together in this fashion, they define a particular machine. *In re Nuijten*, 500 F.3d 1346 (Fed. Cir. 2007) (stating that a machine is a "'concrete thing, consisting of parts, or of certain devices and combination of devices.'") This 'includes *every mechanical device* or combination of mechanical powers and devices *to perform some function and produce a certain effect or result*.'" *Id.* at 1355 (citation omitted). This is precisely what the examiner found as the basis for allowance of the '988 Patent, that "prior art of record fails to teach or suggest . . . a computing device specifically comprising the three distinct knowledge bases as recited," which computing device is configured to use the knowledge bases to generate a list of treatment regimens. A1207-A1208.

Finally, the court's view that the "computing device" "appears to be doing nothing more than speeding up the research and mental processes that a doctor normally goes through when evaluating the best treatment options or regimen for a given patient," A29, reflects that the court simply did not understand the nature of computerized expert system technology. Indeed, ABL submitted evidence, which the district court struck from the record, which specifically demonstrated that the claimed invention produces results that consistently improved treatment outcomes

beyond what physicians themselves could do: In short, the claimed invention was not merely faster than doctors, it was better. *E.g.*, A982.

The district court also erred in its application of the transformation prong, finding that claimed "the alleged transformation performed in the defendants' patents is more akin to a manual reorganization of treatment options." A32. The data used in the ABL Patents is nothing like the "public or private legal obligations or relationships, business risks" of *Bilski*, the credit card numbers of *Cybersource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366 (Fed. Cir. 2011), the "deedshares" in *Fort Properties, Inc. v. American Master Lease LLC*, 671 F.3d 1317 (Fed. Cir. 2012), or the "business or legal relationships" of *In re Ferguson*, 558 F.3d 1359 (Fed. Cir. 2009). Instead, it is precisely what the Court in *Bilski* approved: data "representative of physical objects or substances"—patients and drugs. Thus, the ABL patent claims satisfy the transformation prong as well.

III. INVALIDATION OF ALL CLAIMS OF TWO PATENTS AND UNASSERTED CLAIMS BASED ON ANALYSIS OF ONE CLAIM IS AN ERROR OF LAW

The district court made an additional error of law by invalidating all claims of both of the ABL patents based on an analysis of only claim 1 of the '786 patent. First, it was an error to invalidate unasserted patent claims, over which no case or controversy existed between the parties and therefore no jurisdiction existed for the district court to make such a ruling. Second, having only evaluated the eligibility

of a single *independent* claim of *one* patent, the court erred in invalidating *dependent* claims and claims of the *other* patent. Even assuming *arguendo* that the district court's conclusion on patent eligibility was correct, this Court should narrow the impact of that decision because the district court improperly enlarged its jurisdictional power to invalidate patent claims.

A. The District Court Lacked Jurisdiction to Invalidate Unasserted Claims

The only claims of ABL's patents that have ever been at issue in this declaratory judgment action, as SG has acknowledged, are claims 1 and 23 of each patent. *See* A368 at ¶ 5 ("In this litigation, ABL is only asserting claims 1 and 23 of the '786 patent."), *id.* at ¶ 7 ("In this litigation, ABL is only asserting claims 1 and 23 of the '988 patent."); A535-A537 (listing only claims 1 and 23 of each patent as at issue as part of claim construction statement).

As this Court has consistently held, "the existence of a case or controversy must be evaluated on a claim-by-claim basis." *E.g.*, *Jervis B. Webb Co v. So. Sys., Inc.*, 742 F.2d 1388, 1399 (Fed. Cir. 1984); *see also Streck, Inc. v. Research & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1282-83 (Fed. Cir. 2012) (a party "must show a continuing case or controversy with respect to withdrawn or otherwise unasserted claims."). This Court has previously vacated district court rulings on summary judgment invalidating an entire patent when only a subset of claims had been asserted. *E.g.*, *Fox Group, Inc. v. Cree, Inc.*, 700 F.3d 1300, 1307-08 (Fed. Cir.

2012) (vacating district court declaration that entire patent invalid when only two claims had been asserted); *see also Streck*, 665 F.3d at 1283-84 (district court did not have jurisdiction over unasserted claims for purposes of a summary judgment motion on invalidity).

The district court exceeded its jurisdiction by invalidating all claims of each patent when only claims 1 and 23 had been asserted by ABL. It was undisputed that dependent claims 2-22 and 24-44 and "computer program product" claims 45-66 of each patent were never at issue in this case.[12] Accordingly, the Court should

[12] *For the very first time*, SG argued in opposing ABL's motion for reconsideration that there "is a very real controversy regarding the entire '786 and '988 patents" on the basis that ABL uses its patents "in the marketplace in a manner that is significantly injuring Smartgene's business." A2748. SG did not support these statements with any evidence. Nor did it argue in its pleadings or anywhere else that ABL's use of its *own patented technology* somehow created declaratory judgment jurisdiction between the parties. If SG believed there was a case or controversy with respect to all claims of the two ABL patents, it should not have represented that only claims 1 and 23 of each were at issue. *See* A368 at ¶ 5 ("In this litigation, ABL is only asserting claims 1 and 23 of the '786 patent."), *id.* at ¶ 7 ("In this litigation, ABL is only asserting claims 1 and 23 of the '988 patent."); A535-A537 (listing only claims 1 and 23 of each patent as at issue as part of claim construction statement).

vacate the district court's finding of invalidity at least with respect to the unasserted claims.[13]

B. The District Court Erred in Invalidating All Claims of Two Patents Based on an Analysis of One Claim of One Patent

Both 35 U.S.C. § 282 and this Court's jurisprudence make clear that "each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; [and] dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim." *Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1370 (Fed. Cir. 2003) (citing 35 U.S.C. § 282); *see also Sandt Tech. v. Resco Metal & Plastics*, 264 F.3d 1344, 1356 (Fed. Cir. 2001) ("Because dependent claims contain additional limitations, they cannot be presumed to be invalid as obvious just because the independent claims from which they depend have been properly so found."). Accordingly, the district court erred in holding all the claims of both ABL patents invalid on the basis of a single claim, and

[13] In its order denying ABL's motion for reconsideration, the district court erroneously labeled ABL's assertions that only claims 1 and 23 of each patent were at issue "patently false." In support, the district court pointed to SG's declaratory judgment complaint, which alleged generally that each patent was invalid. A141-142 at ¶¶ 20, 26. But the district court failed this court's admonition that there must be a "*continuing* case or controversy." *Streck*, 665 F.3d at 1283. Once it became clear that ABL was only asserting claims 1 and 23 of each patent, the district court was divested of jurisdiction regarding the unasserted claims, any later representations by SG notwithstanding.

particularly when the validity of many claims, including *all* dependent claims, had not been litigated. *See Novo Nordisk Pharm., Inc. v. Bio-Technology Gen. Corp.*, 424 F.3d 1347 (Fed. Cir. 2005) (vacating the portion of the district court's order relating to a claim not litigated).

Claims may only be grouped together for purposes of an invalidity analysis if they involve the same issues of validity and the claim issues are "*substantially materially identical*." *See Dayco*, 329 F.3d at 1370. The district court made no such finding. Instead, the court analyzed only claim 1 of the '786 patent, thereby ignoring differences in the form, type, and limitations of 131 other claims across two different patents. The court stated without explanation that any differences between the method and system claims were immaterial. A3 at n.4. This was error; there are meaningful differences in the particular language of each claim (*e.g.*, element (a) of claim 23 lacks any "means" language under 35 U.S.C. § 112, ¶ 6). *See Dow Chem. Co. v. Mee Indus.*, 341 F.3d 1370, 1375 (Fed. Cir. 2003) (finding that "[n]either the district court in its opinion, nor the parties in their briefs have paid sufficient attention to the specific language of the individual claims). *Even assuming* that the court could group the method, system and computer program product claims into one analysis, no basis appears in the record for the district court to find, for example, that the "computer readable program code

means" limitations of claims 45-66 are "substantially materially identical" to claims *that do not recite* these limitations.

For purposes of subject matter eligibility, dependent claims can introduce the type of "meaningful limitations" necessary to introduce patent eligibility to a claim that otherwise might preempt all practical uses of an abstract idea. *See CLS*, 2013 U.S. App. LEXIS 9493, at *110 (Rader, J., concurring-in-part and dissenting-in-part) ("The patents at issue contain dependent claims which include additional structural and functional limitations that render the system even more concrete."); *id.* at *139 (Moore, J., dissenting-in-part) ("[T]he dependent claims (which are also asserted and must be analyzed individually) limit the computer system even further."). The district court summarily struck the dependent claims without considering at all the impact of their additional limitations on patent eligibility.

Similarly, the court erred in invalidating claims 23-44 of both ABL patents, all of which are apparatus claims containing means for limitations. The court did not construe these claims under § 112(f). *See CLS*, 2013 U.S. App. LEXIS 9493 at *139 (Moore, J., dissenting-in-part) (Means for "claims expressly cover only the algorithm disclosed as a means for performing the acquisition, or equivalents thereof" and should be individually considered for patent eligibility.)

CONCLUSION

On the basis of the foregoing analysis, this Court should rule either that the claims in suit are indeed patent-eligible, or in the very least remand to the district court for discovery and factual development in regards to the interpretation of the claim, and whether evidence clearly and convincingly supports the conclusion that the claims in fact "wholly preempt" "all practical applications" of the abstract idea. This court should also remand for the district court to specifically address the patent eligibility of the unasserted claims.

Dated: June 20, 2013

Respectfully submitted,

FENWICK & WEST LLP

/s/ Robert R. Sachs
Robert R. Sachs

Counsel for Appellants
Advanced Biological Laboratories, SA
and ABL Patent Licensing
Technologies, SARL

ADDENDUM

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

SMARTGENE, INC., Plaintiff, v. ADVANCED BIOLOGICAL LABORATORIES, SA, *et al*., Defendants.	Civil Action No. 08-00642 (BAH) Judge Beryl A. Howell

MEMORANDUM OPINION

Plaintiff SmartGene, Inc., a North Carolina corporation, brought this lawsuit against Defendant Advanced Biological Laboratories, SA, a company with its principal place of business in Luxembourg, seeking declaratory judgment as to the invalidity, unenforceability, and SmartGene's non-infringement of U.S. Patent No. 6,081,786 (the "786 patent") and U.S. Patent No. 6,188,988 B1 (the "988 patent") (collectively, the "patents-in-dispute"). After prolonged litigation, including a stay of proceedings of two and a half years, SmartGene filed a Motion for Partial Summary Judgment, contending that the "patents-in-dispute" are facially invalid under 35 U.S.C. § 101 of the Patent Act because the subject matter is ineligible for patent protection.[1] Defendants, Advanced Biological Laboratories, SA ("ABL SA") and ABL Patent Licensing

[1] SmartGene stated at the March 9, 2012 Motions Hearing that the Motion was framed as a Motion for "Partial" Summary Judgment because the Motion deals only with the validity of the patents-in-dispute and does not address all disputed claims. *See* Motions Hearing Transcript ("Tr") (Rough), Mar. 9, 2012, at 9:30, 42:23-43:1; 43:6-12 (The parties have not requested formal transcripts from the court reporter. Accordingly, the Court's citations to transcripts are from the court reporter's rough draft of the proceedings.). No matter the styling of the pending Motion as a "partial" Motion for Summary Judgment, grant of this Motion is dispositive in this matter since the validity of the patents-in-dispute is the *sine qua non* for all the claims and counterclaims.

Technologies, SARL ("ABL PLT") (collectively "ABL")[2], oppose the Motion for Partial Summary Judgment, arguing that the patents-in-dispute constitute eligible subject matter under 35 U.S.C. § 101. For the reasons explained below, SmartGene's Motion for Partial Summary Judgment is granted and this case is dismissed.

I. FACTUAL AND PROCEDURAL BACKGROUND

A. The Patents

The patents at stake in this dispute are Patent Nos. 6,081,786 (the "786 patent") and 6,188,988 B1 (the "988 patent"), of which the defendants are the undisputed owners. Compl. ¶¶ 7-8.[3] The '786 patent application was filed with the United States Patent and Trademark Office ("PTO") on April 1, 1999, and the patent issued on June 27, 2000. *See* LCvR 7(h) Statement of Material Facts in Support of Pl.'s Mot. for Partial Summ. J. at ¶ 4. The application for the '988 patent, considered a "continuation" of the application for the '786 patent, was filed on March 10, 2000, and the patent issued on February 13, 2001. *Id*. at ¶ 6.

Both patents are entitled "Systems, Methods and Computer Program Products for Guiding the Selection of Therapeutic Treatment Regimens," and relate "to a system, method, and computer program for guiding the selection of therapeutic treatment regimens for complex disorders . . . by ranking available treatment regimens and providing advisory information." Defs.' Mem. in Opp. to Mot. for Partial Summ. J. ("Defs.' Mem."), ECF No. 50, at 1-2. Both patents-in-dispute are based on the same patent specifications and disclosures, and relate to methods (*i.e*., process) and systems for an interactive, computerized program for guiding the

[2] On November 23, 2011, the Court directed that ABL PLT be joined as a defendant in this case pursuant to Federal Rule of Civil Procedure 25(c). *See* Order, ECF No. 43. The Court directed that the party be joined in order to facilitate conduct of the case, because ABL PLT appears to have received rights originally belonging to ABL SA, not because there are distinct, substantive claims against ABL PLT. *See* Minute Order (Jan. 3, 2012).

[3] The operative complaint, and the one cited throughout this Opinion, is the First Amended Complaint filed on May 20, 2008. *See* ECF No. 4.

selection of therapeutic treatment regimens for a patient based on input provided by a physician. *See* Pl.'s Mem. in Support of Mot. for Partial Summ. J. ("Pl.'s Mem."), ECF No. 47, at 3; Defs.' Mem. at 1-2. The defendants sum up their invention as follows: "Element (a) specifies that the physician provide patient information to the computing device which includes prior therapeutic treatment regimen information. This information is then processed against a first knowledge base that contains different treatment regimens and a second knowledge base of expert rules. The computing device then generates available treatments along with advisory information for those treatments. By providing the patient information to the system and allowing interaction with the physician, the Patents describe how therapeutic treatment regimens can be listed with corresponding advisory information." Defs.' Mem. at 11.

The Court's analysis focuses on the patentability of Claim 1 of the '786 patent. The language for Claim 1 in both the '786 and '988 patent is nearly identical. SmartGene asserts that the differences between Claim 1 in the '786 patent and '988 patent are insignificant, and that these first claims are representative of all of the claims of the patents-in-dispute. Pl.'s Mem. at 8 n.3. The defendants failed to contest this characterization in their brief.[4] The Court concludes that the differences between the various method and system claims within the patents-in-dispute are immaterial with respect to whether the patents constitute eligible subject matter under 35 U.S.C. § 101. Accordingly, the pending Motion turns on whether Claim 1 of the '786 patent

[4] Although not raised in their brief, the defendants erroneously asserted at the Motions Hearing that the "method" and "system" claims at issue require a different standard of review for subject matter patentability. Tr. 29:6-30:17. Here, Claim 1 in both the '786 and '988 patents is a method claim, while Claim 23 in both the '786 patent and '988 patent is a system claim. *See* Pl.'s Mem. at 11 nn. 5-6. Specifically, the defendants argued that "for a system claim, there is a little bit different analysis because claiming an actual system . . . makes it even less abstract because it's not just a method . . . [I]t is even more intimately connected to the computer, as it is the system." Tr. 30:4-15. The defendants fail to cite any authority that supports their assertion, and ignore authority to the contrary. *See, e.g.*, *In re Meyer*, 688 F.2d 789, 795 n.3 (C.C.P.A. 1982) ("for purposes of section 101, [claims reciting "means for" performing the steps set forth in the method claims] are not treated differently from method claims").

constitutes eligible subject matter under 35 U.S.C. § 101 of the Patent Act. Claim 1 of the '786 patent is directed to:

> 1. A method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said method comprising:
>   (a) providing patient information to a computing device comprising:
>   a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;
>   a second knowledge base comprising a plurality of expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition;
>   a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and
>   (b) generating in said computing device a ranked listing of available therapeutic treatment regimens for said patient; and
>   (c) generating in said computing device advisory information for one or more therapeutic treatment regimens in said ranked listing based on said patient information and said expert rules.

'786 patent, Col. 17-18, ECF No. 4-1.

B. Procedural History

The litigation between these parties originated in September 2007, when ABL SA filed a lawsuit in the United States District Court for the Eastern District of Texas, Marshall Division, against SmartGene, alleging that SmartGene "manufactures, uses and sells products that infringe the '786 and '988 Patents." Compl. ¶ 9. ABL SA alleged specifically that "Smartgene's IDNS™ HIV program incorporates at least one technology which infringes at least claim 1 of each [of] the '786 and '988 Patents." *Id.* The district court in Texas dismissed the case on April 10, 2008 for lack of personal jurisdiction. *Id.* at 10.

SmartGene commenced this action in the District Court for the District of Columbia against ABL SA on April 11, 2008, seeking declaratory judgment of non-infringement, patent invalidity, and patent unenforceability under the Patent Act, 35 U.S.C. § 1 *et seq.*, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202.[5] SmartGene asserts in its Complaint that the '786 patent and the '988 patent are invalid "for failing to comply with 35 U.S.C. §§ 101-103 and/or 112." Compl. ¶¶ 20, 26.[6]

ABL SA filed its Answer and Counterclaims on October 6, 2008, alleging that SmartGene's products "[incorporate] at least one technology which infringes at least claim 1 of each of the '786 and the '988 patents." Answer, ECF No. 12, at ¶ 42.[7]

On February 3, 2009, SmartGene's unopposed motion to stay this proceeding, *see* ECF No. 18, was granted due to concurrent patent validity reexaminations brought before the PTO. *See* Order, ECF No. 19. Cumulatively, the defendants advise that the PTO held six reexaminations—three for each of the patents-in-dispute—with two reexaminations combined for each patent. Tr. 45:11-13. None of the reexamination proceedings, however, addressed the subject matter eligibility question under 35 U.S.C. § 101. Tr. 45:16. The PTO completed its reexamination proceedings and issued a final non-appealable denial of further review

[5] This Court has jurisdiction to adjudicate this dispute pursuant to 28 U.S.C. § 1331 and 28 U.S.C. § 1338.

[6] SmartGene further claims that "[d]uring Defendant's prosecution of patent applications PCT US9907171 and EP 999166262.1, which claim priority to the application to which the '786 and '988 Patents claim priority, the PCT and European Patent Office ("EPO") search and examination authorities cited prior art references in reports dated October 22, 1999, September 14, 2004, March 9, 2005, October 27, 2005, and March 17, 2006." Compl. ¶ 11. SmartGene claims that the EPO "determined that the EP 999166262.1 application was "not patentable in view of this prior art . . ." Compl. ¶ 12. The prior art utilized to deny the EPO patent was apparently unavailable during the PTO proceedings because the PTO Board of Appeals "said it would not consider those references" in its reexamination proceeding. Tr. 6:4-8. Accordingly, SmartGene claims that this prior art is "material to the patentability of the '786 and '988 Patent claims, and, upon information and belief, renders the '786 and '998 Patents invalid by 35 U.S.C. § 102 and/or § 103." Compl. ¶ 13. This claim is not at issue in the pending motion.

[7] SmartGene asserts that the counterclaim for infringement is invalid because it was asserted by ABL PLT, rather than ABL SA. Pl.'s Mem. at 1 n.1. The Court need not address this issue because the patents are invalid and the counterclaims are moot.

proceedings on June 14, 2011. Joint Motion to Lift Stay, ECF. No. 32, at 1. The PTO concluded that all of the claims of both patents-in-dispute were patentable over the prior art presented during the reexamination. *Id.*

On September 7, 2011, the parties filed a joint motion to lift the stay and submitted a proposed scheduling order. *Id.* This case was then reassigned to the undersigned Judge on September 15, 2011.

This Court lifted the stay on October 21, 2011, and subsequently entered a scheduling order to govern the proceedings in this matter. *See* Minute Order (Oct. 21, 2011); Scheduling Order, ECF No. 39. SmartGene filed the instant Motion for Partial Summary Judgment on December 12, 2011, alleging that the '786 patent and the '988 patent constituted ineligible patent subject matter under 35 U.S.C. § 101 and pursuant to *Bilksi v. Kappos*, 130 S. Ct. 3218 (2010). *See* ECF No. 47. Both parties agree that the resolution of this motion does not depend on the disposition of any facts. Pl.'s Mem. at 2; Tr. 28:10-15.[8]

This Court held a hearing on the Motion for Partial Summary Judgment and a Markman Hearing to resolve disputes over claim construction on March 9, 2012 ("Motion Hearing"). For the reasons explained below, SmartGene's Motion for Partial Summary Judgment is granted.[9]

II. LEGAL STANDARD

A. Summary Judgment

Pursuant to Rule 56 of the Federal Rules of Civil Procedure, summary judgment shall be granted "if the movant shows that there is no genuine dispute as to any material fact and the

[8] While the defendants state in their opposition brief that "there are several issues of material fact that should preclude the granting of summary judgment," *see* Defs.' Mem. at 1, they did not file a separate statement of disputed material facts, as required by Local Civil Rule 7(h), and clarified at the Motions Hearing that there are no outstanding material facts that prevent adjudication of this Motion for Partial Summary Judgment. *See* Tr. 28:10-15.

[9] Since the Court grants summary judgment for SmartGene, the Court need not proceed with claim construction.

movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a); *Anderson v. Liberty Lobby*, 477 U.S. 242, 247 (1986); *Estate of Parsons v. Palestinian Authority*, 651 F.3d 118, 123 (D.C. Cir. 2011); *Tao v. Freeh*, 27 F.3d 635, 638 (D.C. Cir. 1994). Summary judgment is properly granted against a party who, "after adequate time for discovery and upon motion, . . . fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial." *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). The burden is on the moving party to demonstrate that there is an "absence of a genuine issue of material fact" in dispute. *Celotex Corp.*, 477 U.S. at 323.

In ruling on a motion for summary judgment, the court must draw all justifiable inferences in favor of the nonmoving party, and shall accept the nonmoving party's evidence as true. *Anderson*, 477 U.S. at 255; *Estate of Parsons*, 651 F.3d at 123; *Tao*, 27 F.3d at 638. The court is only required to consider the materials explicitly cited by the parties, but may on its own accord consider "other materials in the record." FED. R. CIV. P. 56(C)(3). For a factual dispute to be "genuine," *Estate of Parsons*, 651 F.3d at 123, the nonmoving party must establish more than "[t]he mere existence of a scintilla of evidence" in support of its position, *Anderson*, 477 U.S. at 252, and cannot simply rely on allegations or conclusory statements. *Greene v. Dalton*, 164 F.3d 671, 675 (D.C. Cir. 1999). Rather, the nonmoving party must present specific facts that would enable a reasonable jury to find in its favor. *Id.* If the evidence "is merely colorable, . . . or is not significantly probative, . . . summary judgment may be granted." *Anderson*, 477 U.S. at 249-50 (citations omitted).

B. Subject Matter Patentability under the Patent Act

SmartGene's Motion for Partial Summary Judgment challenges the subject matter eligibility of the patents-in-dispute under 35 U.S.C. § 101. *See* Pl.'s Mot. for Part. Summ. J.

("Pl.'s Mot."), ECF No. 47. Congress has defined which inventions are patentable in Section 101 of the Patent Act, which states in its entirety:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101.

The Patent Act defines the term "process" as "process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." 35 U.S.C. § 100.

The Supreme Court has further elaborated on what constitutes a patentable process claim, noting that

> a process may be patentable, irrespective of the particular form of the instrumentalities used . . . A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing. If new and useful, it is just as patentable as is a piece of machinery.

Diamond v. Diehr, 450 U.S. 175, 182-83 (1981) (quoting *Cochrane v. Deener*, 94 U.S. 780, 787-88 (1877)).

While the Patent Act covers a broad range of subject matter, there are three important subject matter exceptions from patentability: "laws of nature, physical phenomena, and abstract ideas." *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010) ("*Bilski II*") (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)); *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). The Supreme Court has found that these categories of exceptions "are not patentable, as they are the basic tools of scientific and technological work." *Benson*, 409 U.S. at 67. "Thus, the Court has written that a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are manifestations of . . .

nature, free to all men and reserved exclusively to none." *Mayo Collaborative Servs. v. Prometheus Labs*.,132 S. Ct. 1289, 1293 (2012) ("*Prometheus*") (citations and quotation marks omitted). "While these exceptions are not required by the statutory text," the Supreme Court has noted, "they are consistent with the notion that a patentable process must be 'new and useful.' And, in any case, these exceptions have defined the reach of the statute as a matter of statutory *stare decisis* going back 150 years." *Bilski II*, 130 S. Ct. at 3225 (citation omitted). Still, the Supreme Court has recognized that "too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Prometheus*, 132 S. Ct. at 1293. The issue before this Court is whether the patents-in-dispute are abstract such that they do not constitute patentable subject matter. Pl.'s Mem. at 1.

C. Level of Deference to the PTO

Patents issued by the PTO, and their underlying claims, are presumed valid. *See* 35 U.S.C. § 282. "[T]his presumption can only be overcome by clear and convincing evidence to the contrary." *Unique Indus. v. 965207 Alta. Ltd.*, No. 08-1095, 2012 U.S. Dist. LEXIS 19621, at *2 (D.D.C. Feb. 16, 2012); *Eli Lilly & Co. v. Barr Labs*, 251 F.3d 955, 962 (Fed. Cir. 2001); *Apple Computer v. Articulate Sys.*, 234 F.3d 14, 20 (Fed. Cir. 2000).

The determination of whether a claimed invention is invalid for lack of subject matter patentability under 35 U.S.C. § 101 is a "threshold inquiry" and a matter of law. *See In re Bilski*, 545 F.3d 943, 950-51 (Fed. Cir. 2008) ("*Bilski I*"). "[A]ny claim of an application failing the requirements of § 101 must be rejected even if it meets all of the other legal requirements of patentability." *Id*. at 950. The Court may conduct a section 101 analysis before the Court conducts a formal construction of claims. *See Ultramercial, LLC v. Hulu, LLC*, 657 F.3d 1323,

1325 (Fed. Cir. 2011) ("claim construction may not always be necessary for a § 101 analysis"). "Only after an invention has satisfied § 101, will it be analyzed under the remaining hurdles of the Patent Act, which include the requirement that an invention be novel, *see* § 102; nonobvious, *see* § 103; and fully and particularly described, *see* § 112." *CLS Bank Int'l.*, 768 F. Supp. 2d at 221, 233 (citing *Bilski II*, 130 S. Ct. at 3225).

The fact that the PTO conducted reexaminations of the patents-in-dispute does not trigger higher deference on the issue of subject matter patentability because the PTO cannot review subject matter eligibility during a reexamination proceeding. 37 C.F.R. § 1.552. This lawsuit, therefore, is not dealing with matters previously covered during the reexamination proceedings. *Id*. Titled "Scope of reexamination in *ex parte* reexamination proceedings," § 1.552 states, in relevant part, that upon *ex parte* reexamination, the PTO may only examine the contested patent "on the basis of patents or printed publications and, with respect to subject matter added or deleted in the reexamination proceeding, on the basis of the requirements of 35 U.S.C. § 112." It further states that "[i]ssues other than those indicated . . . will not be resolved in a reexamination proceeding. If such issues are raised by the patent owner or third party requester during a reexamination proceeding, the existence of such issues will be noted by the examiner in the next Office action, in which case the patent owner may consider the advisability of filing a reissue application to have such issues considered and resolved." 37 C.F.R. § 1.552. "Thus, other challenges to the patentability of original claims — such as qualification as patentable subject matter under § 101 or satisfaction of the written description and enablement requirements of § 112—may not be raised in reexamination proceedings." *In re NTP*, 654 F.3d 1268, 1275-76 (Fed. Cir. 2011); *see also* 35 U.S.C. § 302 (reexaminations may be conducted on "the basis of any prior art"). Since this issue cannot be raised in a reexamination proceeding, no additional

deference is accorded to the PTO as to subject matter patentability.[10] *See, e.g.*, *In re NTP*, 654 F.3d at 1275-76.

III. DISCUSSION

In its Motion for Partial Summary Judgment, SmartGene contends that the patents-in-dispute constitute ineligible patent subject matter because they are (1) "directed to abstract ideas and mental processes," and because (2) the patents-in-dispute fail the "machine or transformation" ("MOT") test articulated in *Bilski*, and are thus invalid. Pl.'s Mem. at 1. In support of this contention, SmartGene asserts that the patents-in-dispute are "directed to nothing more than a mental process in which a person, *e.g.*, a physician, engages when determining a treatment for a patient suffering from a disease or a medical condition." Pl.'s Mem. at 6.[11]

The defendants respond that (1) the claims at issue are not directed to an abstract idea, and (2) although the MOT test is "not the sole test for patentability," the patents-at-issue satisfy that test. Def.'s Mem. at 7-8. According to the defendants, the patents-in-dispute "describe an interactive system, method, and computer program to assist the physician in keeping track of potential treatment regimens and optionally ranking those regimens based on the patient's personal information." Defs.' Mem. at 1-2. "Rather than supplanting the role of the physician, as SmartGene suggests, the invention seeks to improve patient treatment by giving the physician reference to a program which can exceed his or her own capabilities." *Id*. at 2.

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[10] Procedurally, the parties could have raised with the Court the issue of subject matter patentability before requesting a stay of this patent action pending PTO reexamination proceedings. If that issue had been taken up earlier in this case, the PTO may have been spared six reexaminations of the patents-in-dispute.

[11] As noted, Claim 1 of the '786 patent discloses a "method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition" by: (a) having the user input information into a "computing device" comprised of three databases, including (i) a medical conditions database, (ii) a database containing expert rules for selecting a treatment regimen, and (iii) an advisory information database; (b) having the computing device generate a ranked listing of therapeutic treatment regimens for the patient; and (c) generating advisory information based on patient information and expert rules. *See* '786 Patent, Col. 17-18, ECF No. 4-1.

Guided by Supreme Court and Federal Circuit precedent in this area, the Court proceeds with its analysis by (A) examining 35 U.S.C. § 101 as a "threshold" inquiry into patent validity; (B) reviewing Supreme Court caselaw "guideposts" on the subject of patent subject matter eligibility; and then examining whether the patents-in-dispute (C) satisfy the MOT test, and (D) constitute eligible subject matter irrespective of the MOT test. Finally, although the Court does not formally construct the claims on which there is disagreement between the parties, the Court (E) examines the claim construction proposals to inform its section 101 analysis. The Court concludes that the relevant precedent and tests demonstrate that the patents-in-dispute constitute ineligible subject matter and are thus invalid.

A. 35 U.S.C. § 101 as a Threshold Inquiry Into Patent Validity

As the Supreme Court noted in *Bilski v. Kappos*, the 35 U.S.C. § 101 inquiry is a "threshold test." *Bilski II*, 130 S. Ct. 3218, 3225 (2010). "It is well-established that [t]he first door which must be opened on the difficult path to patentability is § 101." *CLS Bank Int'l. v. Alice Corp. Pty. Ltd.*, 768 F. Supp. 2d 221, 233 (D.D.C. 2011) (citation and quotation marks omitted). A recent Federal Circuit decision, however, cast doubt on this approach, sharply questioning the wisdom of utilizing the § 101 subject matter inquiry as a threshold question. *See MySpace, Inc. v. Graphon Corp.*, No. 2011-1149, 2012 U.S. App. LEXIS 4375 (Fed. Cir. Mar. 2, 2012). In a majority decision, the Federal Circuit cautioned that lower courts should avoid the "swamp of verbiage that is § 101 by exercising their inherent power to control the processes of litigation, . . . and insist that litigants initially address patent invalidity issues in terms of the conditions of patentability defenses as the statute provides, specifically §§ 102, 103, and 112." *Id*. at *24 (internal citation omitted). The decision asserts that this approach would alleviate the necessity of entering "the murky morass that is § 101 jurisprudence." *Id*; *see also Classen*

Immunotherapies, Inc. v. Biogen Idec, 659 F.3d 1057, 1073-75 (Fed. Cir. 2011) (urging judicial restraint in the face of a plethora of section 101 litigation).

Following the Motions Hearing in this case, however, the Supreme Court, in *Mayo Collaborative Servs. v. Prometheus Labs.*, 132 S. Ct. 1289 (2012), clarified that a 35 U.S.C. § 101 subject matter patentability inquiry *is* the threshold analysis for determining patent validity. The Supreme Court explicitly rejected that the "screening function" of 35 U.S.C. § 101 may be performed by determining the novelty, *see* 35 U.S.C. § 102, non-obviousness, *see* 35 U.S.C. § 103, or the adequacy of the written specification, *see* 35 U.S.C. § 112, of a patentable claim. *Id.* at 1303-04. The Court cautioned that "[shifting] the patent-eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty, while assuming that those sections can do work that they are not equipped to do." *Id.* at 1304. Conducting a patent eligibility inquiry under any of the alternative sections "would make the 'law of nature' exception to §101 patentability a dead letter. The approach is therefore not consistent with prior law." *Id.* at 1303; *see also Bilski II*, 130 S. Ct. at 3235; *CLS Bank Int'l.*, 768 F. Supp. 2d at 233; *see also* H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952) ("A person may have 'invented' a machine or a manufacture, which may include anything under the sun that is made by man, but it is not necessarily patentable under section 101 unless the conditions of the title are fulfilled") (quoted in *Prometheus*, 132 S. Ct. at 1303-04). Accordingly, this Court treats the § 101 subject matter patentability inquiry as the threshold inquiry for patent validity. In this case, the section 101 analysis begins and ends the Court's inquiry as it reveals that the patents-in-dispute are not patentable.

B. "Guideposts" for Adjudicating Subject Matter Patentability

The Supreme Court has highlighted a trilogy of its decisions – namely *Gottschalk v. Benson*, *Parker v. Flook*, and *Diamond v. Diehr* – as useful "guideposts" when considering exceptions to patent subject matter eligibility under 35 U.S.C. § 101. *Bilski II*, 130 S. Ct. at 3231. The Court notes that "[i]n searching for a limiting principle, [the Supreme Court's] precedents on the unpatentability of abstract ideas provide useful tools." *Id*. at 3229. The most recent Supreme Court decision on this topic, *Prometheus*, reaffirms the importance of these tools, focusing its section 101 analysis, *inter alia*, on this trilogy of cases as well as *Bilski II*. *See Prometheus*, 132 S. Ct. at 1298-1301. This Court follows suit. The Court reviews these guideposts below, and finds that, under this instructive precedent, the patents-in-dispute are not patent-eligible processes.

1. *Gottschalk v. Benson*

The Supreme Court's decision in *Benson* is the first of these patent subject matter eligibility cases. *Gottschalk v. Benson*, 409 U.S. 63 (1972). There, the Supreme Court held that "a method for converting binary-coded decimal (BCD) numerals into pure binary numerals" that was "not limited to any particular art or technology, to any particular apparatus or machinery, or to any particular end use" was not a process covered by the Patent Act. *Id*. at 64, 71-73. The claimed method sought patent protection over an "algorithm" that represented "a generalized formulation for programs to solve mathematical problems of converting one form of numerical representation to another." *Id*. at 65. The Supreme Court observed that "[t]he mathematical formula involved here has no substantial practical application except in connection with a digital computer, which means that if the judgment below is affirmed, the patent would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." *Id*. at

71-72. The Court expressed concern that "the 'process' claim is so abstract and sweeping as to cover both known and unknown uses," which could "vary from the operation of a train to verification of drivers' licenses to researching the law books for precedents" and "be performed through any existing machinery or future-devised machinery or without any apparatus." *Id*. at 68. Accordingly, the Supreme Court denied the claim and found that computer algorithms that encompass methods for mathematical conversion are "procedure[s] for solving a given type of mathematical problem" and are ineligible patent subject matter that erroneously seeks to patent the "basic tools of scientific and technological work." *Id*. at 67.

2. *Parker v. Flook*

"In *Flook*, the Court considered the next logical step after *Benson*." *Bilski II*, 130 S. Ct. at 3230. There, the patent-holder asserted patent rights protection over a "method for updating alarm limits," which indicated the point at which the catalytic conversion conditions in the petrochemical and oil-refining industries can produce inefficiencies or danger. *Parker v. Flook*, 437 U.S. 584, 585. As the Court noted, "[t]he only novel feature of the method is a mathematical formula." *Id*. "In [*Benson*], we held that the discovery of a novel and useful mathematical formula may not be patented. The question in this case is whether the identification of a limited category of useful, though conventional, post-solution applications of such a formula makes respondent's method eligible for patent protection." *Id*. The Court found that the "only difference between the conventional methods of changing alarm limits and that described in respondent's application rests in the second step – the mathematical algorithm or formula" and that "a claim for an improved method of calculation, even when tied to a specific end use, is unpatentable subject matter under § 101." *Id*. at 595 & n.18.

Moreover, the Court found that incorporation of "post-solution" activity did not render the formula patentable, because a "competent draftsman could attach some form of post-solution activity to almost any mathematical formula." *Id*. at 590. The Court rejected the idea that post-solution activity, "no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process," finding that would "[exalt] form over substance." *Id*. The Pythagorean theorem, for example, would not have been patentable even if a final step had been added "indicating that the formula, when solved, could be usefully applied to existing surveying techniques." *Id*. The patent thus constituted ineligible subject matter because the claim sought patent protection over an improved method for computing alarm limits, which were otherwise computable by hand. *Id*. As the Court explained in *Diehr* and *Bilski II*, "*Flook* stands for the proposition that the prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula to a particular technological environment' or adding 'insignificant postsolution activity.'" *Bilski II*, 130 S. Ct. at 3230 (quoting *Diehr*, 450 U.S. at 191-92).

3. *Diamond v. Diehr*

In *Diehr*, the Supreme Court "established a limitation on the principles articulated in *Benson* and *Flook*." *Bilski II*, 130 S. Ct. at 3230. The Court upheld as patentable subject matter a process for molding, or "curing," raw synthetic rubber into a product that would retain its shape. This process involved using the well-known components of time, temperature and a mathematical formula, but combined them with a previously uncontrollable variable (*i.e.*, the temperature inside of a rubber press) and use of a programmed computer. *Diamond v. Diehr*, 450 U.S. 175, 187 (1981). When implemented in a series of steps, the claimed process took the "guess work" out of the proper curing time. Although the invention incorporated a well-known

mathematical formula, the Supreme Court concluded that the patent constituted eligible subject matter because it sought process protection over the formula's use solely in conjunction with the other steps of the process. *Id*. "These other steps apparently added to the formula something that in terms of patent law's objectives had significance – they transformed the process into an inventive application of the formula." *Prometheus*, 132 S. Ct. at 1299.

Unlike in *Benson*, where the "sole practical application of the algorithm was in connection with the programming of a general purpose digital computer," *Diehr*, 450 U.S. at 185-86, the claimed invention in *Diehr* used a mathematical equation tied to "all of the other steps in their claimed process," which itself was limited to curing synthetic matter. *Id.* at 187. The Supreme Court acknowledged that although, "[o]bviously, one does not need a 'computer' to cure natural or synthetic rubber," when the computer significantly reduces the probability of damaging the rubber, the process is not rendered unpatentable solely because of the use of a mathematical formula or computer. *Id.*

The Supreme Court articulated the following guidance: "A mathematical formula as such is not accorded the protection of our patent laws [citing *Benson*], and this principle cannot be circumvented by attempting to limit the use of the formula to a particular technological environment [citing *Parker*]. Similarly, insignificant post-solution activity will not transform an unpatentable principle into a patentable process. *Ibid*." *Diehr*, 450 U.S. at 191-92. The Court went on to say, however, that, "when a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (*e.g.*, transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101." *Id*. at 192.

4. *Bilski II*

In *Bilski II*, the Supreme Court held that the trilogy of cases discussed above – *Benson*, *Flook*, and *Diehr* – made "clear that petitoner's application [for a business method for hedging risk in the energy commodities market] is not a patentable process." 130 S. Ct. at 3231 (quotation marks omitted). The Court stated that the patent application sought protection over a "fundamental economic practice long prevalent in our system of commerce and taught in any introductory finance class." *Id*. at 3231 (citation omitted). The Court found that "[t]he concept of hedging, described in claim 1 and reduced to a mathematical formula in claim 4, is an unpatentable abstract idea, just like the algorithms at issue in *Benson* and *Flook*. Allowing petitioners to patent risk hedging would preempt use of this approach in all fields, and would effectively grant a monopoly over an abstract idea." *Id*. The Court drew this conclusion "narrowly on the basis of this Court's decisions in *Benson*, *Flook*, and *Diehr*, which show that petitioners' claims are not patentable processes because they are attempts to patent abstract ideas." *Id*. at 3229-30.

5. *Prometheus*

The most recent guidance from the Supreme Court on section 101 analysis concerns patent claims covering a process aimed to aid doctors administering thiopurine drugs to treat patients with autoimmune disease. "The claims purport to apply natural laws describing the relationships between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects." *Mayo Collaborative Servs. v. Prometheus Labs., Inc*., 132 S. Ct. 1289, 1294 (2012). In *Prometheus*, the Court concluded, based on the Court's precedent detailed above, that the process claims were directed to natural law and were thus unpatentable.

Specifically, the *Prometheus* Court distilled the guideposts from its earlier section 101 cases into the following "warnings." The Supreme Court warned "against interpreting patent statutes in ways that make patent eligibility 'depend simply on the draftsman's art' without reference to the 'principles underlying the prohibition against patents for [natural laws],'" *id.* (quoting *Flook*, 437 U.S. at 593), and warned against "upholding patents that claim processes that too broadly preempt the use of a natural law." *Id*. (citing *O'Reilly v. Morse*, 56 U.S. 62, 112-120). A "process that focuses upon the use of a natural law" must "contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Id*. (quoting *Flook*, 437 U.S. at 594). The Court found that the patent at issue failed this test, explaining that "the steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Id*. The Court further observed that "upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries," and thereby allowing monopolies of unforeseeable scope. *Id*.

6. ***Patents-in-Dispute Are Unpatentable Abstract Ideas Under Supreme Court Precedent***

This Court finds that, as in *Benson*, *Flook*, *Bilski II*, and *Prometheus*, the "patent application here can be rejected under [the Supreme Court's] precedents . . ." *Bilski II*, 130 S. Ct. at 3231. Mental processes and abstract intellectual concepts are simply not patentable for the sound reason that "monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it." *Prometheus*, 132 S. Ct. at 1293. The patents-in-dispute do no more than describe just such an abstract mental process engaged in

routinely, either entirely within a physician's mind, or potentially aided by other resources in the treatment of patients.

Specifically, the claim here, like the claim in *Prometheus*, "presents a case for patentability that is weaker than the (patent-eligible) claim in *Diehr* and no stronger than the (unpatentable) claim in *Flook*." *Id*. at 1299. In *Diehr*, as noted, the parties sought patent protection over the use of a mathematical equation "in conjunction with all of the other steps in their claimed process. These include[d] installing rubber in a press, closing the mold, constantly determining the temperature of the mold, constantly recalculating the appropriate cure time through the use of the formula and a digital computer, and automatically opening the press at the proper time." *Diehr*, 450 U.S. at 187. The Court found that the invention was patentable under section 101 because it was not "an attempt to patent a mathematical formula, but rather [was] an industrial process for the molding of rubber products." *Id*. at 192. Unlike the patent-eligible claim in *Diehr*, the claim at issue here, as described below, involves no "transformation of an article" nor a "step-by-step method for accomplishing such [transformation]."[12] *Id*. at 184. The claim here is more like the claim in *Flook* (and *Prometheus*) because it is merely a recitation of abstract steps, rather than an innovation that adds something "specific to the laws of nature [or abstract ideas] other than what is well-understood, routine, conventional activity, previously engaged in by those in the field." *Prometheus*, 132 S. Ct. at 1299.

The claims at issue here are also analogous to the claim in *In re Meyer*, 688 F.2d 789 (C.C.P.A. 1982), a case before the United States Court of Customs and Patent Appeals. There, the patent applicant sought patent protection over a process for gathering neurological testing data, imputing it into a computer, and using a formula to infer whether certain neurological

[12] The Court discusses this concept of transformation more fully below in the discussion of the "machine or transformation" test.

elements are functioning. *In re Meyer*, 688 F.2d at 793. The United States Court of Customs and Patent Appeals rejected the patent owner's assertion that the invention was "concerned with replacing, in part, the thinking processes of a neurologist with a computer," and instead concluded that, "the process recited is an attempt to patent a mathematical algorithm rather than a process for producing a product as in [*Diehr*]." *Id*. at 794. Here, the defendants have stated that "the purpose of [their] invention was to provide the practitioner with help, to give the practitioner more than he could have just in his mind." *See* Tr. 35:16-18. This Court rejects this argument where the patents-in-dispute are even more abstract than in *Meyer*, which at least involved a mathematical algorithm.[13]

Before proceeding to the machine-or-transformation test that the Supreme Court has highlighted as an "important tool" in section 101 analysis, the Court first examines the '786 patent step-by-step in the context of the Court's precedent, as the Court did in *Prometheus*. Set against this binding precedent, the Court concludes that nothing in Claim 1 of the '786 patent transforms the everyday abstract ideas on which it is based into patentable processes.

a. An Examination of Each Step in Claim 1 of the '786 Patent

"[W]hen a court examines whether a claim is directed to an abstract idea, the court must view each claim as a whole." *CLS Bank Int'l v. Alice Corp. Pty, Ltd.*, 768 F. Supp. 2d 221, 232 (D.D.C. 2011). The Court views Claim 1 as a whole but still finds it useful to examine the claim in steps for the purposes of its analysis of the claim as a whole. The first step of Claim 1 of the '786 patent describes "[a] method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said method comprising." As SmartGene highlights, the language of the claim is directed to "nothing more than a mental process . . ."

[13] The defendants were given the opportunity to distinguish *In Re Meyer* at the Motions Hearing and were unable to do so, with counsel for the defendants simply reiterating counsel's view of the purpose and function of the invention at issue here, rather than specifically addressing how this case is distinguishable from *Meyer*. Tr. 34:22-35:25.

Pl.'s Mem. at 6. In fact, this process is one that is performed in doctors' offices everyday. A doctor speaks with a patient, who describes his or her ailments. The doctor recalls or looks up possible treatment regimens, and then advises the patient about the treatment regimen options, and the doctor's recommendation for the patient. Indeed, the patent specification itself admits that the invention "can simulate the judgment and behavior of a human or organization that has expert knowledge and experience in a particular field." '786 patent, Col. 7, lines 47-49.

The second step of Claim 1 of the '786 patent addresses "(a) providing patient information to a computing device comprising [three knowledge databases]." The Court sees nothing in this step that is any different than the process a doctor goes through in real time when a doctor evaluates a patient by taking a medical history and obtaining information pertinent to the patient's condition and documenting the same in a medical chart. Similarly, the patents' reference to three databases also mimics the evaluative process involved in the treatment of patients. Specifically, after collecting patient information, a doctor would consider "therapeutic treatment regimens for said disease or medical condition" (as in the first knowledge base), consult "expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition" (as in the second knowledge base), and review "advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens" (as in the third database). The claim itself does not add anything to the process that doctors regularly engage in mentally when evaluating and treating patients.

The next step of Claim 1 of the '786 patent is "(b) generating in said computing device a ranked listing of available therapeutic treatment regimens for said patient." The Court views this step as describing what goes on in the mind of a doctor in evaluating and ranking possible treatment options for a patient based upon the benefits and counter-indicators of each option.

The final step of Claim 1 of the '786 patent is "(c) generating in said computing device advisory information for one or more therapeutic treatment regimens in said ranked listing based on said patient information and said expert rules." The Court understands this step as corresponding to a doctor generating a treatment plan for a patient.

b. An Examination of Claim 1 of the '786 Patent As A Whole

In essence, these four steps describe abstract ideas that are commonly performed by medical professionals in evaluating, considering and constructing treatment options for a patient presenting a specific medical condition. As with the claim examined in *Prometheus*, these "steps consist of well understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons [this Court believes] that the steps are not sufficient to transform unpatentable [abstract ideas] into patentable applications . . . ." *Prometheus*, 132 S. Ct. at 1298. In short, the claims track the abstract mental processes of a doctor treating a patient. Accordingly, analyzing Claim 1 of the '786 patent under the Supreme Court's precedent, this Court finds that the claims of the patents-in-dispute are abstract ideas and unpatentable.

C. Claims are Invalid under the Machine-or-Transformation Test

The Court also finds that the patents-in-dispute are invalid under the "machine-or-transformation" or "MOT" test utilized in some of the Supreme Court and Federal Circuit precedent. Different tests have been employed over time to analyze claims under section 101. *See, e.g.*, *State St. Bank & Trust Co. v. Signature Fin. Group*, 149 F.3d 1368, 1373 (Fed. Cir. 1998) (finding that a transformation "constitutes a practical application of a mathematical algorithm, formula, or calculation, because it produces 'a useful, concrete and tangible result'").

The most recent test developed in *Bilski I* is the MOT test. The Federal Circuit, sitting *en banc* in *Bilski I*, articulated the standards for determining whether a claimed method constituted a patentable "process" under section 101. There, the Federal Circuit clarified that the "machine-or-transformation" test was the "governing test" for determining patent eligibility under section 101. *In re Bilski*, 545 F.3d 943, 955-56 (Fed. Cir. 2008).

In *Bilski II*, the Supreme Court notably rejected the Federal Circuit's decision that the "machine or transformation" test was the "sole test for governing § 101 analysis." 130 S. Ct. at 3227. The Court found that while "[i]t is true that patents for inventions that did not satisfy the machine-or-transformation test were rarely granted in earlier eras . . . times change." *Id*. The Court reflected generally that "[w]ith ever more people trying to innovate and thus seeking patent protections for their inventions, the patent law faces a great challenge in striking the balance between protecting inventors and not granting monopolies over procedures that others would discover by independent, creative application of general principles." *Id*. at 3228. The Court, however, did not foreclose the use of the machine-or-transformation test. *Id*. at 3227. Indeed, while the Supreme Court emphasized that the MOT test is "not the sole test for deciding whether an invention is a patent-eligible 'process,'" the Court noted that the Supreme Court's "precedents establish that the [MOT] test is a useful and important clue, an investigative tool, for determining whether some claimed inventions are processes under § 101." *Id*. Most recently, in *Prometheus*, the Supreme Court rejected not the MOT test but the Federal Circuit's application of that test. There, the Federal Circuit concluded that the transformation prong of the MOT test was satisfied because the claimed process involved "transforming the human body by administering a thiopurine drug and transforming the blood by analyzing it to determine the metabolite levels." *Prometheus*, 132 S. Ct. at 1302. The Court described as "irrelevant" the

transformation on which the Federal Circuit upheld the patent at issue since no part of the so-called "transformation" required the claimed process. *Id*. Accordingly, this Court employs the MOT test as a useful investigative tool.

Under the MOT test, a process claim is patentable if "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Bilski I*, 545 F.3d at 954; *see also Flook*, 437 U.S. at 589 n. 9 ("An argument can be made [that the Supreme Court] has only recognized a process as within the statutory definition when it either was tied to a particular apparatus or operated to change materials to a different state or thing.") (internal quotation marks and citations omitted). The "use of a specific machine or transformation of an article must impose meaningful limits on the claim's scope to impart patent-eligibility" and, furthermore, "the involvement of the machine or transformation in the claimed process must not merely be insignificant extra-solution activity." *CLS Bank Int'l*, 768 F. Supp. 2d at 234 (citations and quotation marks omitted). SmartGene claims that the patents-in-dispute "[a]ll fail" the MOT test because (1) "they are not tied to a particular machine or apparatus that imparts meaningful limitations on the claims" and (2) "they do not transform a particular article into a different state or thing." Pl.'s Mem. at 11. The defendants argue, in response, that "[e]ven though the [MOT] test is no longer preferred for inventions of the Information Age," *see Ultramercial*, 657 F.3d at 1327, "the invention of the Asserted Claims satisfies both prongs of the test." Defs.' Mem. at 10. The Court first addresses the machine prong and then the transformation prong, and finds that the patents-in-dispute do not satisfy either one of them. The Court also finds that the computing device referenced by the claims does not impose any meaningful limit on the scope of the claims.

1. *Claims of the Patents-in-Dispute Are Not Tied to a Particular Machine*

To satisfy this prong, a claimed process must be "tied to a particular machine or apparatus." *Bilski I*, 545 F.3d at 954. SmartGene argues that "[t]he claims of the patents-in-suit are essentially methods for providing and generating information, and do not identify a particular machine for performing the recited claim steps. While the claims reference a 'computing device,' this generic token reference does not identify any particular machine or provide any indication of what particular type of machine is to be used . . ." Pl.'s Mem. at 12. The defendants argue in response that the claims meet the machine prong of the MOT test "because the claims are tied to a particular machine that has [three databases]" and "[i]t can hardly be argued that the computing device is incidental to the invention, rather the computing device allows the invention to pull information from three databases." Defs.' Mem. at 12-13. The Court finds that the patents-in-dispute do not satisfy the machine prong for two reasons.

First, the claims of the patents-in-dispute do not refer to any "particular" machine. While the claims reference a "computing device," these references are insufficient to satisfy the machine test. The defendants argue that "the figures and specification specify how the computer is to be specially programmed to implement the method covered by the Asserted Claims," but the Court is not persuaded. Defs.' Mem. at 13. [14] The patents-in-dispute include no special programming code, nor provide any specific algorithms that the computers would use to perform the database matching or synthesis of expert rules, advisory information, treatment regimens, and

[14] Counsel for the defendants made an argument at the Motions Hearing that "figure one, a flow-chart" may be "considered [an algorithm]." Tr. 36:23-37:3. The chart simply shows boxes labeled with descriptions of the data and the verbs "generate," "provide," "examine," "enter," and "modify." The Court is not at all convinced that the flow chart in figure one is an "algorithm," and counsel has provided no authority for this figurative leap. Counsel further argues that "under the system description there is a lengthy discussion of the system architecture, the essential server, the local server and exactly what steps are carried out to perform the method [in columns 7, 8, 9, 10]. So although [there] wasn't any code that was included in the patent, there doesn't have to be code for there to be an algorithm disclosed in the specification." Tr. 39:8-14. SmartGene argues in response that columns 7 through 10 do not contain an algorithm. Tr. 43:19-22. The Court agrees.

patient information. Moreover, unlike in *Ex Parte Brown*, Appeal 2009-012201, 2011 Pat. App. LEXIS 15902 (BPAI Feb. 8, 2011), on which the defendants rely, *see* Defs.' Mem. at 9-10, there is no specific "server" specified in the claims.

To the extent that the claims reference a machine at all, they reference a "general purpose computer," which does not satisfy the machine prong. *See, e.g.*, *CLS Bank Int'l.*, 768 F. Supp. 2d at 237 ("With evolving guidance on this issue, district courts have determined that a method claim that is directed to a general purpose computer is not tied to a particular machine under the MOT test.") (citations omitted); *Graff/Ross Holdings LLP v. Fed. Home Loan Mortg. Corp.*, No. 07-796, 2010 U.S. Dist. LEXIS 141399, at *20 (D.D.C. 2010) (finding that a "computer processor" referenced in method claim is not a "particular machine" under the MOT test); *Accenture Global Services, GMBH v. Guidewire Software, Inc.*, 691 F. Supp. 2d 577, 597 (D.Del. 2010) ("data processing system", "claim folder", "display device", and "screen" referenced in claim did not constitute a "particular machine" for the purposes of the MOT test); *see also* ECF No. 55, Ex. A, July 8, 2009 Office Action for Patent Application No. 10/857, 105 ("105 Application") (application where the PTO found that the term "computing device" did not refer to a particular machine and rejected claims on that basis). [15]

The defendants argue that the Court should look to *VS Techs, LLC v. Twitter, Inc*., No. 2:11-cv-43, 2011 U.S. Dist. LEXIS 114998 (E.D. Va. Oct. 4, 2011), as "[a] good example of the

[15] SmartGene notes that the difference between the '105 Application and the patents-in-dispute "is that the PTO applied the MOT test to the claims of the '105 Application and not to the patents-in-suit as the MOT was not the law at the time the patents-in-suit issued." Pl.'s Reply at 7. PTO states as a reason for the rejection of claims in the '105 Application: "Claims 1-15 remain rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory matter. This is a new grounds of rejection necessitated by the recent decision in [*In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008)]. . . In the instant case, the method claims are not so tied to another statutory class of invention because the method steps that are critical to the invention are 'not tied to any **particular apparatus** or **machine**' and therefore do not meet the machine-or-transformation test . . . The instantly recited 'computing device' is not a specific computing device and the claims are therefore non-statutory. The rejection could be overcome by reciting a 'suitably programmed computing device' or 'appropriately programmed computing device' provided such is supported in the specification as originally filed." ECF No. 55, Ex. A at 2-3 (emphasis in original). PTO may have come to the same conclusion if it had examined the patents-in-dispute under the same criteria.

proper application of the machine prong . . ." Defs.' Mem. at 12. There, the court found that a claim satisfied the machine prong because "the patent constitutes a practical application of an idea." *VS Techs, LLC*, 2011 U.S. Dist. LEXIS 114998, at *14-15. The Court finds, to the contrary, that the caselaw is clear that allowing a process to become patentable simply because it is computer aided and constitutes a practical application would render the subject-matter eligibility criteria contained in section 101 meaningless. *See Dealertrack, Inc. v. Huber*, Nos., 2012 WL 164439, at *16 (concluding that claims drawn to a "computer-aided" method of processing information through a clearinghouse were ineligible abstract ideas under section 101); *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1375 (Fed. Cir. 2011) (emphasizing "that the basic character of a process claim drawn to an abstract idea is not changed by claiming only its performance by computers, or by claiming the process embodied in program instructions on a computer readable medium").

Furthermore, the fact that the '786 claim relies in part on four other patents for its inference database does not save the defendants' claim under section 101. The defendants argued at the Motions Hearing that "the means plus function language is relevant [to the machine prong analysis], because it provides even further support that the claims are intimately tied to the computer for as you know, for means plus function language, we have to disclose the structure." Tr. 39:16-20. In turning to the defendants' proposed claim construction of the term "means for generating," which they cited at the Motions Hearing to satisfy the machine prong of the MOT test, the Court notes that the defendants propose the following construction: "Inference engine and its equivalents." Defs.' Cl. Constr. Br., ECF No. 54, at 6. The defendants describe the "corresponding structure" as follows:

> The inference engine 26 may be implemented as hardware, software, or combinations thereof. Inference engines are known and any of a variety thereof

> may be used to carry out the present invention. Examples include, but are not limited to, those described in U.S. Pat. No. 5,263,127 to Barabash et al. (Method for fast rule execution of expert systems); U.S. Pat. No. 5,720,009 to Kirk et al. (Method of rule execution in an expert system using equivalence classes to group database objects); U.S. Pat. No. 5,642,471 to Paillet (Production rule filter mechanism and inference engine for expert systems); U.S. Pat. No. 5,664,062 to Kim (High performance max-min circuit for a fuzzy inference engine).

Defs. Cl. Constr. Br. at 6 (quoting, *inter alia*, '786 patent, Col. 8, lines 25-37). The Court finds that general references to other patents as "examples" of components of a structure without any detail as to implementation or combination is simply insufficient to identify a structure in the claims. This is fatal for the defendants' claims. Accordingly, the Court finds that nothing in the defendants' proposed claim construction helps them satisfy the "machine" prong of the MOT test.

Second, the computing device referenced in the claims is incidental to the claimed invention and is not used for more than "insignificant postsolution activity," and thus does not satisfy the machine prong. *Diehr*, 450 U.S. at 191. As in *Flook*, the computing device is merely a means of improving an existing process, which does not make the claims of the patents-in-dispute patentable. *Flook*, 437 U.S. at 595 n. 18. Indeed, when a computer is functioning simply to speed up a process, this does not make the process patentable. *CLS Bank Int'l*, 768 F. Supp. 2d at 238-39 ("In order for the addition of a machine to impose a meaningful limit on the scope of a claim, it must play a significant part in permitting the claimed method to be performed, rather than function solely as an obvious mechanism for permitting a solution to be achieved more quickly"); *see also Cybersource*, 654 F.3d at 1375-76 (case would be different if "as a practical matter, the use of a computer [was] required"). In the patents-in-dispute, the computing device referenced in the claims appears to be doing nothing more than speeding up the research and mental processes that a doctor normally goes through when evaluating the best treatment

options or regimen for a given patient. Thus, Claim 1 of the '786 patent does not satisfy the machine prong of the MOT test.

2. *Claims of the Patents-in-Dispute Do Not Satisfy the Transformation Test*

To satisfy the "transformation" prong of the MOT test, a claimed process must "[transform] a particular article into a different state or thing." *Bilski I*, 545 F.3d at 954. SmartGene argues that the claims of the patents-in-dispute "merely take one form of information (i.e., patient information, therapeutic treatment regimens and advisory information) and represent it in a different form (i.e., lists of therapeutic treatment regimens and advisory information)" and that "[s]uch manipulations of information . . . are insufficient to meet the 'transformation' prong of the MOT." Pl.'s Mem. at 16. The defendants counter that "raw patient information is transformed into a treatment regimen which in turn transforms the patient's body." Defs.' Mem. at 11. According to the defendants, this "system creates the ability for a physician to interact with a program and view and develop a treatment regimen for a patient." *Id*. This Court finds the defendants' arguments unavailing and concludes that the patents do not satisfy the transformation prong of the MOT test.

The Supreme Court and Federal Circuit have offered some guidance in deciphering whether a process satisfies the transformation prong. First, the "transformation must be central to the purpose of the claimed process" *see Bilski I*, 545 F.3d at 962, and the "mere manipulation or reorganization of data . . . does not satisfy the transformation prong." *CyberSource*, 654 F.3d at 1375. Second, "[p]urported transformations or manipulations simply of public or private legal obligations or relationships, business risks, or other such abstractions cannot meet the test because they are not physical objects or substances, and they are not representative of physical objects or substances." *Bilski I*, 545 F.3d at 963. Finally, as noted, the Supreme Court in

Prometheus recently rejected the Federal Circuit's application of "transformation," where the Federal Circuit concluded that claimed processes were patent eligible where they involved "transforming the human body." *Prometheus*, 132 S. Ct. at 1302-1303. The Supreme Court in *Prometheus*, however, did not retreat from a transformation analysis as part of a subject matter patentability test under section 101.

The Federal Circuit's guidance in *CyberSource* is particularly instructive. In *Cybersource*, the Federal Circuit held that a method for detecting credit card fraud in internet commerce constituted ineligible patent subject matter. *Id*. There, the parties sought patent protection over a process that compares databases comprised of credit card transaction history information to determine whether current purchases are indicative of credit card users' purchasing habits. 654 F.3d at 1367. The Federal Circuit concluded that such an invention does not constitute patent eligible subject matter because it "can be performed by human thought alone . . ." *Id.* at 1373. The Federal Circuit also explicitly stated that the mere use of the internet does not create patentable subject matter, because the internet is utilized as a "source of data," and "mere [data-gathering] step[s] cannot make an otherwise nonstatutory claim statutory." *Id.* at 1370 (quoting *In re Grams*, 888 F.2d 835, 840 (Fed. Cir. 1989)). The Federal Circuit found that the patents-in-dispute did not satisfy the transformation prong because "[t]he mere manipulation or reorganization of data . . . does not satisfy the transformation prong." *See CyberSource*, 654 F.3d at 1375. This conclusion indicates that even if computers simplify data gathering and computation functions, a claimed invention is nevertheless unpatentable if it may be entirely performed through mental processes.

Examining the Supreme Court and Federal Circuit precedent, as well as decisions in this Circuit, the Court concludes that, the '786 patent does not involve transformation. As in *Bilski*,

Cyberspace, and *CLS Bank Int'l*, the alleged transformation performed in the defendants' patents is more akin to a manual reorganization of treatment options. This does not satisfy the transformation prong of the MOT test. *See, e.g.*, *CLS Bank Int'l*, 768 F. Supp. 2d at 234-35 (rejecting argument that "would convert almost any use of a computer, or other electronic device with memory, to a transformation under the MOT test simply because data would necessarily have to be manipulated . . . .") (citations omitted).

The defendants' arguments to the contrary are not persuasive. Specifically, the defendants note that the Federal Circuit, in *Bilski I*, stated that "the transformation of . . . raw data into a particular visual depiction of a physical object on a display was sufficient to render that more narrowly-claimed process patent-eligible" and that "the electronic transformation of the data itself into a visual depiction . . . was sufficient." *See* Defs.' Mem. at 11 (quoting *Bilski*, 545 F.3d at 963 (referring to *In re Abele*, 684 F.2d 902 (C.C.P.A. 1982)). Defendants' reliance on *Abele* is misplaced. In *Abele*, the patent applicant sought to patent a process for improving the accuracy and reliability of CAT scan imaging techniques, while simultaneously reducing the X-ray exposure of the patient. *Abele*, 684 F.2d 902, 903 (C.C.P.A. 1982). This process of improving imaging is very different than the data manipulation at issue here. Unlike in *Abele*, the patents here do not manifest any sort of physical transformation, and therefore do not satisfy the transformation prong of the MOT. [16]

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[16] The defendants further rely on an Eastern District of Virginia decision, *VS Techs., LLC v. Twitter, Inc.*, No. 2:11-cv-43, 2011 U.S. Dist. LEXIS 114998, at *19 (E.D. Va. Oct. 4, 2011), where the court noted that a claim directed to the creation of an online community "involves a transformation in the sense that it creates the ability for people to interact in real time." The defendants argue that "[i]n the same way the technology in [*VS Tech*] involved a transformation by creating the ability to interact in real time, the Asserted Claims involve a transformation by creating the ability for the user to interact with the program to develop a treatment regimen." Defs.' Mem. at 11-12. The Court does not find this argument convincing as there is nothing in the Supreme Court or Federal Circuit precedent that suggests data matching and ranking, as described in the patents-in-dispute, constitute a "transformation" of that data in a manner that would satisfy the machine or transformation test. Similarly, the argument by the defendants that their invention "transforms the patient's body," *see id*. at 11, appears to be exactly the type of transformation expressly rejected by the Supreme Court in *Prometheus*.

D. Patent Claims Do Not Constitute Eligible Subject Matter

A claimed method may still constitute eligible subject matter despite failing to satisfy the MOT test. *See Bilski II*, 130 S. Ct. at 3226. The defendants assert that the MOT test is "disfavored," and that the Court should instead be guided by the Federal Circuit's reasoning in *Ultramercial, LLC v. Hula, LLC*, 657 F.3d 1323, 1329 (Fed. Cir. 2011). Defs.' Mem. at 8. An examination of this Federal Circuit precedent, however, only reaffirms that the defendants' patents-in-dispute are abstract and do not constitute patent eligible subject matter.

In *Ultramercial*, the Federal Circuit held that a patent claiming a method for "distributing copyrighted products (e.g. songs, movies, books) over the Internet where the consumer receives a copyrighted product for free in exchange for viewing an advertisement, and the advertiser pays for the copyrighted content," constituted patentable subject matter. 657 F.3d at 1324. The Federal Circuit upheld the patent-eligibility of the mechanism, concluding that this patent "does not claim a mathematical algorithm, a series of purely mental steps, or any similarly abstract concept." *Id*. at 1329. Rather, it "claims a particular method for collecting revenue from the distribution of media products over the Internet." *Id*. This invention constituted patentable subject matter because the claim itself required complex computer programming and "controlled interaction with a consumer via an Internet website." *Id.* at 1330. Unlike the claims in *Cybersource*, the Federal Circuit concluded that the claims here were "something far removed from *purely* mental steps." *Id*. at 1329-1330 (emphasis in original).

While the claims in *Ultramercial* could not be performed as "purely mental steps," and involved a number of steps, with complex computer programming, the defendants' claimed inventions can be performed – and, in fact, are routinely performed – in the minds of physicians who are evaluating patients and selecting therapeutic treatment options for them. The patents-

in-dispute are thus more like the claimed invention in *CyberSource* – a process for detecting credit card fraud in Internet transactions – which the court concluded could be performed exclusively in the human mind. *See CyberSource*, 654 F.3d at 1373. As in *CyberSource*, the claims at issue involve the "organization of data" and do "not require the method to be performed by a particular machine . . ." *Id*. at 1370. The claims thus suffer from the same defects as the claims in *CyberSource* and are not patentable.

The Federal Circuit's recent decision in *DealerTrack* only reinforces that the patents-in-dispute are not patentable. There, the Federal Circuit found that a process for automating credit applications by receiving credit applicant data from a source and then forwarding the data to potential creditors and forwarding the reply data to the first source, constituted ineligible patent subject matter because it sought to "'[explain] the basic concept' of processing information through a clearing-house, just as claim 1 in *Bilski II* '[explained] the basic concept of hedging.'" *DealerTrack, Inc. v. Huber*, Nos. 2009-1566, 2009-1588, 2012 U.S. App. LEXIS 1161, at *47 (Fed. Cir. Jan. 20, 2012) (quoting *Bilski II*, 130 S. Ct. at 3231). The Federal Circuit held that the claim was abstract because the method did not "impose meaningful limits on the claim's scope." *Id.* at *48 (quoting *Bilski I*, 545 F.3d at 961-62). In so holding, the Federal Circuit rejected the assertion that a computer was critical to the process because "the computer here 'can be programmed to perform very different tasks in very different ways[.]'" *Id.* at *48 (quoting *Aristocrat Techs. Australia PTY Ltd. v. Int'l Game Tech.*, 521 F.2d 1328, 1333 (Fed. Cir. 2008)). Thus, "it does not play a significant part in permitting the claimed method to be performed." *Id*. (citations and quotation marks omitted). The Federal Circuit found the patent invalid because the claims were "silent as to how a computer aids the method, the extent to which a computer aids the method, or the significance of a computer to the performance of the method." *Id*. at *48. In

addition, the claims did "not require a specific application" nor were they "tied to a particular machine." *Id*. at 49.

In light of this precedent, the Court finds that the defendants' claims mirror the mental processes that a physician performs, and therefore embody the "'basic tools of scientific and technological work' that are free to all men and reserved exclusively to none." *CyberSource*, 654 F.3d at 1373 (quoting *Benson*, 409 U.S. at 67). Furthermore, the computing device references in the defendants' patents may be "programmed to perform very different tasks in very different ways," and therefore cannot serve as a significant limitation or constraint on the claimed invention. *DealerTrack*, 2012 U.S. App. LEXIS 1161, at *48 (quoting *Aristocrat*, 521 F. 3d at 1333). Like the courts in *Cybersource* and *DealerTrack*, the Court finds the defendants' invention unpatentable.[17]

E. Claim Construction

Finally, while it is not necessary for this Court to formally construct the claims, the Court notes that the defendants' proposed construction of the disputed claims only reinforces that the

[17] SmartGene argues that another reason the patents-in-dispute are unpatentable is that the patents are directed to software *per se*. Pl.'s Mem. at 13; Pl.'s Reply at 2. Specifically, SmartGene points to the language of the '786 patent specification, which states that the invention may be constituted in ". . . an entirely software embodiment. . ." Pl.'s Mem. at 13 (quoting Ex. A., '786 patent, Col. 4, lines 17-20). SmartGene argues that "[s]uch lack of structure renders the claims unpatentable as directed to software *per se*. *Id*.; see also *Ex. Parte Lection*, Appeal No. 2009-012445, 2011 Pat. App. LEXIS 21213, *4 (BPAI Aug. 10, 2011) ("As such, claim 1 encompasses software per se and is therefore directed to nonstatutory subject matter."); *Ex Parte Barbee*, Appeal No. 2009-009777, 2011 Pat. App. LEXIS 20090, at *3 (BPAI June 21, 2011) ("An embodiment that is software per se falls outside of the scope of § 101"); *Ex parte Liebl*, Appeal No. 2009-010624, 2010 Pat. App. LEXIS 14403 (BPAI Mar. 16, 2010) (finding that "the subject matter of the claims on appeal may be properly considered to directly and indirectly recite abstract logic, data structures or software per se which our earlier noted case law considers not to be within in any statutory category within 35 U.S.C. § 101"); *Ex Parte Venkata*, Appeal 2009-007302 n.1, 2010 Pat. App. LEXIS 18234, at *8 (BPAI Oct. 6, 2010) (noting that the specification "indicates that the service discovery functions performed by the recited agents may be implemented in software, firmware, hardware or a combination thereof" and thus finding "that the claimed agents comprised in the service discovery system can exist solely in software" and that "[r]eciting descriptive material *per se* (e.g., data structures and computer programs) . . . is non-statutory."). The defendants do not directly address SmartGene's software *per se* argument in their brief. When given an opportunity to respond to SmartGene's software *per se* argument at the Motions Hearing, the defendants argued, *inter alia*, that "the software *per se* objection is mainly one that has been used in the context of prosecution, and is not a doctrine that has been relied on in the court's recent jurisprudence in the 101 issue." Tr. 31:19-22. Since this software *per se* objection is not necessary to resolve in this Motion, the Court declines to address it.

defendants' claims are unpatentable. The claimed steps of the invention, and not the specification, must "impose meaningful limits on the claim's scope," *see Bilski I*, 545 F.3d at 961-62, in order to cabin the claimed invention's potential reach. The claim language in Claim 1 of the '786 patent fails to enforce any meaningful limits on the scope and breadth of the claimed invention. The defendants propose, for example, that the term "patient information" in Claim 1 of the '786 patent needs no definition. While SmartGene proposes constructing the claim "patient information" to include "gender, age, weight, CD4+ cell information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, information for drug treatments for other conditions, historical information on prior therapeutic treatment regimens for a disease or medical condition, and prior patient information," the defendants insist that the plain language of the claim should apply. Defs.' Cl. Constr. Br. at 2. Likewise, SmartGene proposes that the term "knowledge base" be narrowly constructed to, at a minimum, limit the three databases to human medical information.[18] *Id*. at 3. The defendants decline any narrow construction and instead propose constructing the term "knowledge base" in Claim 1 of the '786 patent simply as "database." *Id*. Thus, the contours of these patents with no definition as to which information is pertinent, combined with the broadest possible construction of the terms, could encompass far more than the common understanding of therapeutic treatment regimens and could, for example, include financial information about the patient and the most economic treatment options available. This is reminiscent of the situation in *Benson*, as discussed *supra*, where the Supreme

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[18] Specifically, SmartGene proposed that "[t]he term 'first knowledge base' should be construed as a database of information accumulated from a body of knowledge of human specialists in the field of therapeutic treatment regimens. The term 'second knowledge base' should be construed as a database of information distinct from the first knowledge base, wherein the second knowledge base is accumulated from a body of knowledge of human specialists in the field of expert rules. The term 'third knowledge base' should be construed as a database of information distinct from the first knowledge base and the second knowledge base, wherein the third knowledge base is accumulated from a body of knowledge of human specialists in the field of advisory information." Defs.' Cl. Constr. Br. at 3.

Court expressed concern that a claim was "so abstract and sweeping as to cover both known and unknown uses," which could "vary from the operation of a train to verification of drivers' licenses to researching the law books for precedents" and "be performed through any existing machinery or future-devised machinery or without any apparatus." *Benson*, 409 U.S. at 68. Indeed, the breadth of these proposed constructions only underlines the abstractness of Claim 1 of the '786 patent. The defendants' claims are "invalid as being directed to an abstract idea preemptive of a fundamental concept or idea that would foreclose innovation in this area." *DealerTrack*, 2012 U.S. App. LEXIS 1161, at * 47; *see also MySpace, Inc. v. Graphon Corp.*, 2012 U.S. App. LEXIS 4375, at *39 (Fed. Cir. Mar. 2, 2012) (J. Mayer, dissenting) (noting that patent claims over "abstract" concepts "fall outside the ambit of section 101 because they are *too* useful and *too* widely applied to possibly form the basis of any patentable invention").

IV. CONCLUSION

For the reasons discussed above, this Court finds that the defendants' Patent Nos. 6,081,786 and 6,188,988 B1 constitute ineligible subject matter under 35 U.S.C. § 101, and are therefore invalid. Accordingly, SmartGene's Motion for Partial Summary Judgment, ECF No. 47, is granted. Since the patents at issue are invalid, the remaining claims and counterclaims pending in the suit are dismissed. An Order consistent with this Opinion shall be filed.

DATED: March 30, 2012

/s/ *Beryl A. Howell*
BERYL A. HOWELL
United States District Judge

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

SMARTGENE, INC., Plaintiff, v. ADVANCED BIOLOGICAL LABORATORIES, SA, *et al*., Defendants.	Civil Action No. 08-00642 (BAH) Judge Beryl A. Howell

ORDER

Upon consideration of the Complaint in this case, the pending motion, the related legal memoranda, and the applicable law, it is hereby

ORDERED that, for the reasons set forth in the accompanying Memorandum Opinion, the plaintiff's Motion for Partial Summary Judgment, ECF No. 47, is GRANTED; it is further

ORDERED that, since the patents at issue are invalid, the remaining claims and counterclaims pending in the suit are dismissed.

SO ORDERED.

This is a final, appealable order.

DATED: March 30, 2012

/s/ Beryl A. Howell
BERYL A. HOWELL
United States District Judge

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

SMARTGENE, INC., Plaintiff, v. ADVANCED BIOLOGICAL LABORATORIES, SA, *et al*., Defendants.	Civil Action No. 08-00642 (BAH) Judge Beryl A. Howell

ORDER

Upon consideration of the Amended Complaint in this case, the pending motions, the related legal memoranda, and the applicable law, it is hereby

ORDERED that the Defendants' Motion for Reconsideration Under F.R.C.P. 59(e), ECF No. 67, is DENIED; and it is further

ORDERED that the Plaintiff's Motion to Strike the Declarations and Certain Exhibits Attached to Defendants' Motion for Reconsideration, ECF No. 68, is GRANTED.

SO ORDERED.

DATED: January 3, 2013

Digitally signed by Beryl A. Howell
DN: cn=Beryl A. Howell, o=District Court for the District of Columbia, ou=United States District Court Judge, email=Howell_Chambers@dcd.uscourts.gov, c=US
Date: 2013.01.03 18:39:34 -05'00'

BERYL A. HOWELL
United States District Judge

This is a final, appealable Order.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

SMARTGENE, INC., Plaintiff, v. ADVANCED BIOLOGICAL LABORATORIES, SA, *et al*., Defendants.	Civil Action No. 08-00642 (BAH) Judge Beryl A. Howell

MEMORANDUM OPINION

Defendants Advanced Biological Laboratories, SA and ABL Patent Licensing Technologies, SARL (collectively "ABL") have filed a Motion for Reconsideration under Federal Rule of Civil Procedure 59(e), *see* ECF No. 67, requesting that this Court reconsider its Order granting summary judgment of patent invalidity in favor of Plaintiff SmartGene, Inc. For the reasons explained below, the three grounds proffered by the defendants for reconsideration are unavailing, and the motion is denied.

I. FACTUAL AND PROCEDURAL BACKGROUND[1]

Plaintiff SmartGene, Inc., a North Carolina corporation, brought this lawsuit against defendant Advanced Biological Laboratories, SA, a company with its principal place of business in Luxembourg, seeking declaratory judgment as to the invalidity, unenforceability, and SmartGene's non-infringement of U.S. Patent No. 6,081,786 (the "786 patent") and U.S. Patent No. 6,188,988 B1 (the "988 patent") (collectively, the "patents-in-suit"). *See* First Am. Compl.

[1] The Court incorporates by reference the detailed factual and procedural background set forth in its Memorandum Opinion, ECF No. 65. *See SmartGene, Inc. v. Advanced Biological Labs., SA*, 852 F. Supp. 2d 42, 45-48 (D.D.C. 2012).

for Declaratory Judgment ("Am. Compl."), ECF No. 4. After prolonged litigation, including a consensual stay of proceedings of two and a half years, *see* Order, ECF No. 19 (dated February 3, 2009), granting plaintiff's unopposed motion to stay, SmartGene filed a Motion for Partial Summary Judgment, contending that the "patents-in-suit are facially invalid as directed to non-statutory subject matter under 35 U.S.C. § 101." Pl.'s Mot. for Part. Summ. J. of Invalidity Under 35 U.S.C. § 101 ("Pl.'s Mot. for Part. Summ. J."), ECF No. 47.[2]

This Court granted the plaintiff's Motion for Partial Summary Judgment, finding that "the defendants' Patent Nos. 6,081,786 and 6,188,988 B1 constitute ineligible subject matter under 35 U.S.C. § 101, and are therefore invalid." *SmartGene, Inc. v. Advanced Biological Labs., SA*, 852 F. Supp. 2d 42, 68 (D.D.C. 2012).

Following the Court's decision, the defendants moved for reconsideration under Federal Rule of Civil Procedure 59(e), and submitted in support of that motion over 1500 pages of declarations and exhibits, including materials not previously provided to the Court for consideration. *See* Defs.' Mot. for Reconsideration Under F.R.C.P. 59(e) ("Defs.' Mot."), ECF No. 67. The plaintiff SmartGene, Inc. opposes the defendants' Motion for Reconsideration, *see* Pl.'s Opp'n to Defs.' Mot. for Reconsideration Under F.R.C.P. 59(e) ("Pl.'s Opp'n"), ECF No. 69, and has moved to strike the declarations and exhibits attached to the defendants' Motion for Reconsideration, *see* Pl.'s Mot. to Strike the Declarations and Certain Exhibits Attached to

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[2] As the Court explained in its Memorandum Opinion regarding this motion,

> SmartGene stated at the March 9, 2012 Motions Hearing that the Motion was framed as a Motion for "Partial" Summary Judgment because the Motion deals only with the validity of the patents-in-dispute and does not address all disputed claims. *See* Motions Hearing Transcript ("Tr") (Rough), Mar. 9, 2012, at 9:30, 42:23-43:1; 43:6-12 . . . . No matter the styling of the pending Motion as a "partial" Motion for Summary Judgment, grant of this Motion is dispositive in this matter since the validity of the patents-in-dispute is the *sine qua non* for all the claims and counterclaims.

SmartGene, Inc., 852 F. Supp. 2d at 45 n.1. The Court cited to the court reporter's rough draft of the proceedings in the Memorandum Opinion because the parties had not yet requested formal transcripts. *See id*.

Defs.' Mot. for Reconsideration ("Pl.'s Mot. to Strike"), ECF No. 68. Both the defendants' Motion for Reconsideration and the plaintiff's Motion to Strike are now pending before the Court.[3]

II. STANDARD OF REVIEW

"'A Rule 59(e) motion is discretionary and need not be granted unless the district court finds that there is an intervening change of controlling law, the availability of new evidence, or the need to correct a clear error or prevent manifest injustice.'" *Messina v. Krakower*, 439 F.3d 755, 758 (D.C. Cir. 2006) (quoting *Firestone v. Firestone*, 76 F.3d 1205, 1208 (D.C. Cir. 1996)). A motion for reconsideration under Rule 59(e) is "'not simply an opportunity to reargue facts and theories upon which a court has already ruled.'" *Fresh Kist Produce, LLC v. Choi Corp.*, 251 F. Supp. 2d 138, 140 (D.D.C. 2003) (quoting *New York v. United States*, 880 F. Supp. 37, 38 (D.D.C. 1995)). Moreover, "the reconsideration and amendment of a previous order is an unusual measure." *Swedish Am. Hosp. v. Sebelius*, 845 F. Supp. 2d 245, 250 (D.D.C. 2012); *see also Jung v. Ass'n of Am. Med. Colls.*, 184 Fed. Appx. 9, 13 (D.C. Cir. 2006) (noting "the high standard for relief under Rule 59(e)"); *Niedermeier v. Office of Max S. Baucus*, 153 F. Supp. 2d 23, 28 (D.D.C. 2001) ("Motions under [Rule 59(e)] are disfavored and relief from judgment is granted only when the moving party establishes extraordinary circumstances."). "Rule 59 was not intended to allow a second bite at the apple." *Oceana, Inc. v. Evans*, 389 F. Supp. 2d 4, 8 (D.D.C. 2005). "In addressing the claims of a party on a motion for reconsideration, the Court is free to expand upon or clarify the reasons supporting its prior ruling." *Bristol-Myers Squibb Co. v. Kappos*, Nos. 09-cv-1330, 09-cv-2420, 2012 U.S. Dist. LEXIS 134299, at *9 (D.D.C. Sept. 20, 2012).

[3] The defendants requested oral argument on their Motion for Reconsideration, *see* ECF No. 67 at 1. Since the parties have extensively briefed the pending motions, however, the Court exercises its discretion under Local Civil Rule 7(f) to decide the motions on the papers.

III. DISCUSSION

The defendants argue that reconsideration of this Court's Order granting summary judgment for Plaintiff SmartGene, Inc. "is necessary for three reasons." Defs.' Brief in Supp. of its Mot. for Reconsideration Under F.R.C.P. 59(e) ("Defs.' Brief"), ECF No. 67-1, at 1. First, the defendants argue that the Court erred in "invalidating all claims of the patents-in-suit, including unasserted claims." *Id.* Second, the defendants argue that "invalidating every claim of both patents, or even the four asserted claims, based solely on an analysis of claim 1 of the '786 patent is an error of law." *Id.* Third, the defendants argue that this Court's ruling "is premised on a clear error of fact and law given that there was a change in controlling law subsequent to the summary judgment proceedings in this case," namely the Supreme Court's decision in *Mayo Collaborative Servs. v. Prometheus Labs., Inc*., 132 S. Ct. 1289 (2012), which the defendants argue they should have been "provided an opportunity to brief." Defs.' Brief at 1. In connection with this third argument, the defendants have submitted evidence that "ABL seeks to present given the *Prometheus* Court's holdings," *id*. at 7, in the form of a declaration from a named inventor of the patents-in-suit, a declaration of a patent attorney involved in prosecuting the patents-in-suit, and hundreds of pages of related exhibits. *See* ECF Nos. 67-4, 67-5, 67-6, 67-7, 67-8, 67-9, 67-10, 67-11, 67-12, 67-13, 67-14, 67-15, 67-16, 67-17, 67-18, 67-19, 67-20, 67-21, 67-22, 67-23, 67-24, 67-25, 67-26, 67-27, 67-28, 67-29, and 67-30 (totaling over 1500 pages). The Court addresses these arguments *seriatim* below.

First, the Court turns to the defendants' contention that "invalidating all claims of the patents-in-suit, including unasserted claims, is an error of law." Defs.' Brief at 1. The defendants claim that it is "undisputed that SmartGene chose to contest the validity of only claims 1 and 23 of each of the '786 and '988 patents" and that the plaintiff "provided no

argument regarding any claims other than the four claims at issue, and never alleged a case or controversy existed with respect to any other claims." *Id.* at 2; *see also id.* at 3 ("In short, there was never a case or controversy with respect to anything but claims 1 and 23 of the '786 and '988 patents."). The defendants' assertions in this regard are patently false, however. The plaintiff made it abundantly clear that it was seeking declaratory judgment of invalidity as to the '786 patent and the '988 patent. *See, e.g.*, Am. Compl., ECF No. 4, at 4 (seeking, in Count II, "Declaratory Judgment of Invalidity of the '786 Patent"); *id.* at ¶ 20 ("The '786 Patent is invalid for failing to comply with 35 U.S.C. §§ 101-103 and/or 112"); *id.* at 5 (seeking, in Count IV, "Declaratory Judgment of Invalidity of the '988 Patent"); *id.* at ¶ 26 ("The '988 Patent is invalid for failing to comply with 35 U.S.C. §§ 101-103 and/or 112"); *id.* at 6 (requesting, in Prayer for Relief, "A declaration that each of the claims of the '786 Patent are invalid" and "A declaration that each of the claims of the '988 Patent are invalid."); Pl.'s Mot. for Clarification and/or Reconsideration, ECF No. 44, at 1 (noting that "[i]n April 2008, SmartGene filed its original Complaint (Dkt# 1) in this declaratory judgment action seeking a declaration that U.S. Patent Nos. 6,081,786 and 6,188,988 B1 (collectively, the 'patents-in-suit') are invalid and that SmartGene does not infringe the patents-in-suit."); Pl.'s Mot. for Part. Summ. J. of Invalidity Under 35 U.S.C. § 101 ("Pl.'s Mot"), ECF No. 47, at 1 ("[T]he patents-in-suit are facially invalid as directed to non-statutory subject matter under 35 U.S.C. § 101."); LCvR 7(h) Statement of Undisputed Material Facts in Supp. of Pl.'s Mot. for Part. Summ. J. of Invalidity Under 35 U.S.C. § 101 ("Pl.'s Facts"), ECF No. 47-1, at 1 (noting that the plaintiff "filed this declaratory judgment action seeking a declaration that U.S. Patent Nos. 6,081,786 and 6,188,988 B1 (collectively, the 'patents-in-suit' and individually as 'the '786 patent' and 'the '988 patent', respectively) are invalid and unenforceable"); Pl.'s Mem. in Supp. of Part. Summ. J. of Invalidity

Under 35 U.S.C. § 101 ("Pl.'s Mem."), ECF No. 47-2, at 1 ("SmartGene filed this declaratory judgment action seeking a declaration that U.S. Patent Nos. 6,081,786 and 6,188,988 B1 (collectively, the 'patents-in-suit') are invalid and that SmartGene does not infringe the patents-in-suit."); *id.* ("SmartGene now moves for summary judgment of invalidity of the claims of the patents-in-suit on the ground that the claims are directed to non-statutory subject matter under 35 U.S.C. §101"); *id.* (arguing that "*all of the claims* of the patents-in-suit are invalid and this motion should be granted") (emphasis added); *id.* at 2 (noting that "[t]his motion, if granted, is dispositive of the validity of the patents-in-suit"); *id.* at 10 (arguing that "the claims of the patents-in-suit are clearly directed to subject matter that is ineligible for patenting and summary judgment of invalidity should be granted"); *id.* at 16-17 ("For the reasons stated above, the claims of the '786 patent and the '988 patent are invalid for failure to claim patent-eligible subject matter."); Pl.'s Reply to Defs.' Opp'n to Pl.'s Mot. for Part. Summ. J. of Invalidity Under 35 U.S.C. § 101 ("Pl.'s Reply"), ECF No. 55, at 1 (concluding that the defendants' opposition "reinforces the compelling case for finding that the *patents-in-suit* are invalid as failing to comply with 35 U.S.C. § 101") (emphasis added); *id.* at 11 ("Regardless of how the claims of the patents-in-suit are analyzed, whether under the software *per se* rubric, the mental steps rubric, or the machine or transformation test, they are abstract. Accordingly, this Court should grant SmartGene's motion and invalidate the claims of the patents-in-suit.").

Rather incredibly in the face of these statements in the record, the defendants characterize as "*undisputed* that SmartGene chose to contest the validity of only claims 1 and 23 of each of the '786 and '988 patents," and aver, in particular, that the plaintiff "never argued the invalidity of dependent claims 2-22, 24-44, nor the invalidity of claims 45-66 of both patents, claims directed to various 'computer program products.'" Defs.' Brief at 2-3 (emphasis added).

Ignoring the plain breadth of the plaintiff's challenge to the validity of the patents-in-suit, the defendants myopically point to the plaintiff's statement that "[t]he following comprises the text of the four claims in suit reproduced in their entirety" together with the plaintiff's listing of claims 1 and 23 of the '786 and '988 patents, and suggest that "SmartGene acknowledged that '[i]n this litigation, ABL is only asserting claims 1 and 23 of the '988 patent . . . .'" *Id.* at 2 n.1. While the LCvR 7(h) Statement of Undisputed Material Facts in Support of Plaintiff's Motion for Partial Summary Judgment, ECF No. 47-1 — to which the defendants never responded — does focus on those four claims, *see* Pl.'s Facts at ¶¶ 5, 7, 9, 10, plaintiff SmartGene consistently asserted that it was contesting the validity of *all of the claims* in both the '786 patent and the '988 patent. *See, e.g., id.* at ¶ 1 (noting that SmartGene "filed this declaratory judgment action seeking a declaration that U.S. Patent Nos. 6,081,786 and 6,188,988 B1 (collectively, the 'patents-in-suit' and individually as 'the '786 patent' and 'the '988 patent', respectively) are invalid and unenforceable"). In fact, the plaintiff made clear that it believed that claim 1 of the '786 patent "is representative of *all of the claims* of the patents-in-suit," Pl.'s Mem. at 8 n.3 (emphasis added), and that, based on a finding of invalidity of claim 1 of the '786 patent, the patents-in-suit were thus invalid. While the defendants may not *agree* that the plaintiff was correct in asserting that claim 1 of the '786 patent was representative of "all of the claims of the patents-in-suit," or in requesting declaratory judgment that the patents-in-suit in their entirety were invalid, the defendants' assertion that "SmartGene provided *no* argument regarding any claims other than the four claims at issue, and never alleged a case or controversy existed with respect to any other claims," Defs.' Brief at 2 (emphasis added), is simply disingenuous in the face of the above-cited statements in the plaintiff's filings.

In any case, the defendants had the opportunity to contest these arguments in their Opposition to the Plaintiff's Motion for Partial Summary Judgment, and failed to do so. *See generally* Defs.' Opp'n to SmartGene's Mot. for Part. Summ. J of Invalidity Under 35 U.S.C. § 101, ECF No. 50.

Even if the defendants somehow did not understand from the plaintiff's motion and the Amended Complaint that the plaintiff was contesting all of the claims in the patents-in-suit based on an analysis of claim 1 of the '786 patent, the Court explicitly brought this issue to the attention of the defendants at the motions hearing held on the plaintiff's Motion for Partial Summary Judgment by asking the defendants' counsel directly the following question:

> THE COURT: Let me clarify one other thing that I promised I was going to ask you . . . . You know, because SmartGene does say that for purposes of this Section 101 Analysis that claim 1 of 786 Patent is representative of *all the claims of the patents in suit*, you didn't really address that in your brief. So I wanted to know if that's your position.

Transcript of Oral Argument ("Tr.") (Mar. 9, 2012), ECF No. 70, at 31, lines 11-17 (emphasis added). The defendants' counsel responded, stating:

> That is not our position. As SmartGene mentioned, and I don't remember if it was their opening brief or their reply brief, there are two different types of claims at issue in the case, both method claims and system claims. And we believe there would be a different analysis as to abstractness issue and whether it can all be performed in the mind between a method claim and a system claim.

Id. at lines 18-24.[4]

[4] The Court asked the defendants' counsel for further explanation of "how the analysis under 101 would differ for each of the four claims, if that's what you think I have to do." Tr. at 32, lines 5-6. The defendants' counsel responded as follows:

> Okay. And to clarify, for purposes of this argument we are not arguing that kind of the different kind of steps that are performed are different. It's mainly focused on the method versus the system claim, because cases such as *Bilski*, when they are talking of business method patents, and things that can be completed entirely in the mind, are method patents. That's what they discussed. So you can perform this method entirely in your mind. Not this method, but the method at *Bilski* for example. And for a system claim, there is a little bit different analysis because claiming an actual system, I would argue, makes it even less abstract because it's not just a method where, okay, we will look at who is performing the method, how do you perform the method, and what's

As the Court noted in its Memorandum Opinion, the defendants' counsel's response to this question at the motions hearing provided the Court no reason to conclude that claim 1 of the '786 patent was *not* representative of all of the claims of the patents-in-suit. *See SmartGene, Inc.*, 852 F. Supp. 2d at 46 n.4 (noting that the defendants "fail to cite any authority that supports their assertion [that "method" and "system" claims require a different standard of review for subject matter patentability], and ignore authority to the contrary") (citing *In re Meyer*, 688 F.2d 789, 795 n.3 (C.C.P.A. 1982) ("for purposes of section 101, [claims reciting "means for" performing the steps set forth in the method claims] are not treated differently from method claims"). Thus, the defendants had the opportunity to address this issue at the motions hearing, and could have provided additional briefing if they believed that the Court had an incorrect understanding of the plaintiff's position. They failed to do so before, during and even after the motions hearing, and have made only a last gasp effort to address the issue of whether claim 1 in both patents-in-suit is representative of all the claims after the Court issued its ruling and in connection with their motion for reconsideration.

The defendants feign ignorance in urging the Court to grant their Motion for Reconsideration, arguing that "[i]f SmartGene truly believed that all the claims of the two patents were a threat, it should have unambiguously argued the invalidity of all claims in its motion." Defs.' Reply Mem. in Supp. of Its Mot. for Reconsideration Under F.R.C.P. 59(e) ("Defs.' Reply"), ECF No. 71, at 1 (emphasis in original). The plaintiff, as indicated above, did just that. *See, e.g.,* Pl.'s Mem. at 2 ("This motion, if granted, is dispositive of the validity of the

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> performing the method, but rather what we have claimed in Claim 23 is a system, the very specific system that is used to select therapeutic treatment regimen[ ]s. It's even less abstract.

Id. at lines 7-23. The Court then responded by asking the defendants' counsel, "And it's less abstract, why?," *id*. at lines 24-25, to which the defendants' counsel responded, "Because it is even more intimately connected to the computer, as it is the system. It's not just a method where arguably – well, they have argued that the computing device as used in the claims can be a human mind." *Id*. at 33, lines 1-4.

patents-in-suit"); *see id.* at 1 ("Accordingly, all of the claims of the patents-in-suit are invalid and this motion should be granted"); Pl.'s Reply at 1 (concluding that the defendants' opposition "reinforces the compelling case for finding that the *patents-in-suit* are invalid as failing to comply with 35 U.S.C. § 101") (emphasis added); *id.* at 11 ("[T]his Court should grant SmartGene's motion and invalidate *the claims* of the patents-in-suit.") (emphasis added); *see also* Am. Compl. at 4 (seeking, in Count II, "Declaratory Judgment of Invalidity of the '786 Patent"); *id.* at ¶ 20 ("The '786 Patent is invalid for failing to comply with 35 U.S.C. §§ 101-103 and/or 112"); *id.* at 5 (seeking, in Count IV, "Declaratory Judgment of Invalidity of the '988 Patent"); *id.* at ¶ 26 ("The '988 Patent is invalid for failing to comply with 35 U.S.C. §§ 101-103 and/or 112"); *id.* at 6 (requesting, in Prayer for Relief, "A declaration that each of the claims of the '786 Patent are invalid" and "A declaration that each of the claims of the '988 Patent are invalid."). That the defendants would not understand from these statements that the plaintiff was challenging each of the claims of the patents-in-suit strains credulity.

Indeed, in its opposition to the defendants' Motion for Reconsideration, SmartGene reaffirms that, in this lawsuit, it "sought a declaration of invalidity of the *entire* '786 and '988 patents." Pl.'s Opp'n at 3 n.2 (emphasis added). The defendants, however, remain adamant in their Reply that "SmartGene does not dispute the critical fact that claims 1 and 23 were the only claims subject to its motion for partial summary judgment." Defs.' Reply at 1. That claim is simply untrue. *See* Pl.'s Opp'n at 3 n.2 (SmartGene asserting that it "sought a declaration of invalidity of the *entire* '786 and '988 patents") (emphasis added). The plaintiff made amply clear its theory of the case, premised on the invalidity of claim 1 of the '786 patent under 35 U.S.C. § 101, and the Court will not reopen the litigation now that the defendants have belatedly realized the implications of the plaintiff's theory, only after issuance of this Court's decision.

See, e.g., Daniel v. Fulwood, No. 10-cv-862, 2012 U.S. Dist. LEXIS 138549, at *4 (D.D.C. Sept. 27, 2012) ("Motions for reconsideration are not simply an opportunity to reargue facts and theories upon which a court has already ruled.") (citations and internal quotation marks omitted).

Accordingly, since the defendants' argument that "[i]nvalidation of [u]nasserted [c]laims [i]s [a]n [e]rror of [l]aw," is based on the false premise that SmartGene "chose to contest the validity of only claims 1 and 23 of each of the '786 and '988 patents," Defs.' Brief at 2, this argument provides no reason for the Court to reconsider its decision.[5]

Second, the Court turns to the defendants' related argument that "invalidating every claim of both patents, or even the four asserted claims, based solely on an analysis of claim 1 of the '786 patent is an error of law." Defs.' Brief at 1.

As a threshold matter, the defendants take issue with SmartGene's argument that SmartGene articulated its claim grouping theory – that claim 1 of the '786 patent was representative of all of the claims in the patents-in-suit – in its Motion for Partial Summary Judgment. *See* Pl.'s Mem. at 8 n.3 ("Accordingly, for the purpose of the § 101 analysis, claim 1 of the '786 patent is representative of all of the claims of the patents-in-suit."). Again, the defendants feign surprise, asserting that, "[i]f this was notice that SmartGene was arguing the invalidity of 127 separate claims — the vast majority of which are dependent claims — then it

[5] The defendants cite a case from the Federal Circuit for the proposition that "[a] party claiming declaratory judgment jurisdiction 'has the burden of showing . . . that there is a substantial controversy, between the parties having adverse legal interests of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.'" Defs.' Brief at 2 (quoting *Streck, Inc. v. Research & Diagnostic Sys.*, 665 F.3d 1269, 1282 (Fed. Cir. 2012). In response, the plaintiff spends much of its opposition to the defendants' Motion for Reconsideration articulating why there was a "very real controversy regarding the entire '786 and '988 patents due to ABL's use of the '786 and '988 patents in the marketplace in a manner that is significantly injuring SmartGene's business." Pl.'s Opp'n at 2. In their reply, the defendants deem to be "irrelevant" SmartGene's allegation that the '786 and '988 patents have been used to ward off SmartGene's potential clients "since the proper inquiry is what SmartGene argued in its motion for summary judgment." Defs.' Reply at 1. Since the Court concludes, from the plain language of SmartGene's Motion for Partial Summary Judgment that SmartGene challenged the patents-in-suit in their entirety, the Court will not proceed here in analyzing SmartGene's allegations of injury in the marketplace as outlined in its opposition to the Motion for Reconsideration.

successfully hid an elephant in a mousehole." Defs.' Reply at 1 n.3. The Amended Complaint and the plaintiff's Motion for Partial Summary Judgment are no "mousehole[s]," however. In those filings, the plaintiff made it crystal clear that it sought nothing less than declaratory judgment as to the invalidity of the '786 and '988 patents, and that it believed that, "for the purpose of the § 101 analysis, claim 1 of the '786 patent is representative of all of the claims of the patents-in-suit." Pl.'s Mem. at 8 n.3. The defendants' argument that it did not have notice of the plaintiff's claim grouping theory is thus unavailing.

The defendants' argument that the grouping of claims was not proper in this case is similarly without merit. The defendants acknowledge that "[c]laims may be grouped together only if they involve the same issues of validity and the claim issues are substantially materially identical." Defs.' Brief at 3 (citing *Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1370 (Fed. Cir. 2003). Yet, the defendants argue that in this case the Court improperly grouped the claims of the '786 and '988 patents together, "thereby ignoring differences in the form, type and limitations of 131 claims in two different patents." Defs.' Brief at 3.

The Court did not ignore the differences, however, but concluded in its Memorandum Opinion that the "differences" between the system and method claims, at least, were "immaterial." *SmartGene, Inc.*, 852 F. Supp. 2d at 46. Specifically, the Court acknowledged SmartGene's assertion that the "differences between Claim 1 in the '786 patent and '988 patent are insignificant, and that these first claims are representative of all of the claims of the patents-in-dispute." *Id.* at 45 (citing Pl.'s Mem. in Supp. of Mot. for Part. Summ. J., ECF No. 47, at 8 n.3). The Court then pointed out that the defendants did not address this assertion *at all* in their opposition brief. *See id.* at 45-46. The Court also pointed out that when the defendants were asked about this issue at the motions hearing, the defendants' counsel answered that, "for a

system claim, there is a little bit different analysis because claiming an actual system . . . makes it even less abstract because it's not just a method . . . [I]t is even more intimately connected to the computer, as it is the system." *Id.* at 46 n.4 (quoting Rough Tr. 30:4-15). The Court rejected this argument, noting that "[t]he defendants fail to cite any authority that supports their assertion, and ignore authority to the contrary." *Id.* (citing *In re Meyer*, 688 F.2d 789, 795 n.3 (C.C.P.A. 1982) ("for purposes of section 101, [claims reciting "means for" performing the steps set forth in the method claims] are not treated differently from method claims").

The defendants now argue that "*even assuming* that the Court could review claims 2-22 and 24-66 of both patents though they were not challenged by SmartGene, there is no basis in the record for the Court to find, for example that the 'computer readable program code means' limitations of claims 45-66 are substantially materially identical to claims *that do not recite* these limitations." Defs.' Brief at 4 (emphasis in original). First of all, the plaintiff *did* challenge these claims, because it challenged the patents-in-suit in their entirety. *See, e.g.*, Pl.'s Mem. at 1 ("SmartGene now moves for summary judgment of invalidity of the claims of the patents-in-suit on the ground that the claims are directed to non-statutory subject matter under 35 U.S.C. §101."). Second, the defendants did not raise these arguments while the plaintiff's Motion for Partial Summary Judgment was pending, and provides the Court no reason to consider them now. As the plaintiff notes, a motion for reconsideration is not an opportunity for "another bite at the apple." *See* Pl.'s Opp'n at 4.[6] Therefore, the Court will not revisit its decision now, when the defendants had the opportunity to address this issue during the summary judgment briefing.

[6] Even in this Motion for Reconsideration, the defendants' briefing is incomplete, and only provides hints of the defendants' argument. The defendants state, in a footnote, without elaboration that, "[w]hile not addressed at the Motions Hearing, the computer program product claims 45-66 for each of the patents would also necessarily require a different standard of review." Defs.' Brief at 4 n.2. The defendants provide no further decoding of this statement for the Court, *i.e.*, to what "different standard of review" they are referring. Again, the defendants have simply provided no reason for this Court to reconsider its decision.

Finally, the Court turns to the defendants' argument that that this Court's ruling is "premised on a clear error of fact and law given that there was a change in controlling law subsequent to the summary judgment proceedings in this case." Defs.' Brief at 1. Specifically, the defendants contend that they should have been "provided an opportunity" to supplement their briefing after the Supreme Court issued its decision in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012), and that, given the change in law, issues of material fact exist that preclude the granting of summary judgment. This argument does not merit this Court's reconsideration of its decision for at least three reasons.

First, as is relevant to this Court's decision in this case, *Prometheus* was not a "change in controlling law." Instead, *Prometheus*, affirmed or clarified earlier Supreme Court precedent related to a 35 U.S.C. § 101 analysis. *See, e.g., SmartGene, Inc.*, 852 F. Supp. 2d at 51 (noting that the Supreme Court in *Bilski v. Kappos*, 130 S. Ct. 3218, 3225, made clear that the 35 U.S.C. § 101 inquiry is a "threshold test," and, despite indications to the contrary by the Federal Circuit, *Prometheu*s "clarified that a 35 U.S.C. § 101 subject matter patentability inquiry *is* the threshold analysis for determining patent validity") (emphasis in original); *SmartGene, Inc.*, 852 F. Supp. 2d at 52 (observing that the Supreme Court in *Bilski* "highlighted a trilogy of its decisions – namely *Gottschalk v. Benson*, *Parker v. Flook*, and *Diamond v. Diehr* – as useful 'guideposts'" and that *Prometheus* "reaffirms the importance of these tools"); *SmartGene, Inc.*, 852 F. Supp. 2d at 55 (finding that, "as in *Benson*, *Flook*, *Bilski II*, and *Prometheus*," the "'patent application here can be rejected under [the Supreme Court's] precedents'") (citation omitted); *SmartGene, Inc.*, 852 F. Supp. 2d at 58 (explaining that pre-*Prometheus*, the Supreme Court "did not foreclose the use of the machine-or-transformation test" and that *Prometheus* "rejected not the MOT test but the Federal Circuit's application of that test"); *SmartGene, Inc.*, 852 F. Supp. 2d at

55 ("The Supreme Court in *Prometheus*, however, did not retreat from a transformation analysis as part of a subject matter patentability test under section 101").

Second, in a related point, *Prometheus* was not determinative of the outcome in this case. Simply stated, this Court's decision would have been the same even if it had been issued before the Supreme Court released its decision in *Prometheus*. The defendants are again disingenuous when they argue that "this Court assumed that the steps recited in the claims were 'well-understood, routine, conventional activity already engaged in by the scientific community' even though the parties never briefed this precise issue." Defs.' Brief at 6. This is just not true. The parties *did* essentially brief this issue. The plaintiff in its Motion for Partial Summary Judgment noted, for example, that "[t]he patents-in-suit . . . claim[ ], in one form or another, mental processes that a person, e.g., a treating physician or consulting physician, performs in selecting a therapeutic treatment regimen for a known disease." Pl.'s Mem. at 3; *see also id*. at 6 ("In effect, the claims of the patents-in-suit are directed to nothing more than a mental process in which a person, e.g., a physician, engages when determining a treatment for a patient suffering from a disease or a medical condition" and "[t]his process is an abstraction, as it is a fundamental task in which a physician engages in his/her mind, each time a patient is treated."); *see id*. at 8-9 (chart describing the human performance equivalent of each claimed method of claim 1 of the '786 patent). The defendants thus had the opportunity to respond in any way they saw fit to the plaintiff's arguments that, *inter alia*, "each limitation of the method claims is readily performable, either entirely mentally within a physician's mind, or potentially with the aid of pencil and paper," Pl.'s Mem. at 7, and that "the steps of claim 1 can be performed in the human mind," *id*. at 9. In fact, they did so in their opposition to that motion, even before the release of *Prometheus*, arguing, for example, that "[o]ne significant advantage provided by the claimed

invention is that a physician has the benefit of more than his or her mind can retain: i.e., the databases can be constantly updated with the most current information in recognition that even the most skilled clinician cannot be expected to know about or memorize every instance of the latest research." Defs.' Opp'n at 2; *see also id.* ("Rather than supplanting the role of the physician, as SmartGene suggests, the invention seeks to improve patient treatment by giving the physician reference to a program which can exceed his or her own capabilities.").[7] This Court analyzed claim 1 of the '786 patent and agreed with the plaintiff in its characterization of the claims of the patents-in-suit. To the extent that the defendants would now like to bolster their arguments with evidence that apparently would have been available to them while the Motion for Partial Summary Judgment was pending, they may not do so.[8]

Finally, the Supreme Court issued its decision on March 20, 2012, and this Court issued its decision on March 30, 2012. Thus, the defendants had ten days in which to apprise the Court of the Supreme Court's decision in *Prometheus*, and how it relates to the instant case, or request an opportunity to brief the case. During that period, the parties provided no notice of supplemental authority regarding *Prometheus*. The defendants now protest that they "never had

[7] The defendants did not at that time suggest, as they do now, that *Diamond v. Diehr* stands for the proposition that "evidence of 'novelty' of any part of a claim is 'of no relevance' for purposes of § 101." Defs.' Opp'n to Pl.'s Mot. to Strike Declarations and Certain Exhibits Attached to Defs.' Mot. for Reconsideration, ECF No. 72, at 2 (quoting *Diamond v. Diehr*, 450 U.S. 175, 189 (1981)). Instead, they simply responded to the plaintiff's arguments with its own, evidently realizing that the Court may consider these arguments in rendering a judgment. The defendants may not now use *Prometheus* as a vehicle for relitigating these arguments, this time with factual support for their arguments.

[8] In connection with the defendants' argument that they should have been given an opportunity to provide supplementary briefing regarding the *Prometheus* decision, the defendants submit with their Motion for Reconsideration over 1500 pages of declarations and exhibits, that the defendants say "would have been submitted if ABL had been given an opportunity to brief Prometheus." Defs.' Brief at 1-2. The plaintiff has filed a Motion to Strike these declarations, as well as the exhibits attached to the declarations, and any reference to them in the defendants' Motion for Reconsideration. *See* ECF No. 68 at 11. Since the Court denies the defendants' Motion for Reconsideration, disagrees with the defendants' contention that there was a change in controlling law, and finds no other reason that the defendants should now be able to supplement the record in this case with evidence that could have been provided before this Court made its decision on the plaintiff's Motion for Partial Summary Judgment, the Court will grant the Plaintiff's Motion to Strike the Declarations and Certain Exhibits Attached to Defendant's Motion for Reconsideration. *See* ECF No. 68.

the opportunity to brief that case." Defs.' Brief at 4. If this were such an important case to the defendants, they could have and should have briefed the case on their own during that period, or at least notified the Court that the case presented new controlling authority about which they wished to provide supplemental briefing. They did not do so, and will not now be allowed to use the *Prometheus* decision as a way to reopen this litigation, particularly when that case was not a change in controlling law with respect to the instant case, and not determinative, but rather only supportive, of this Court's decision in this matter.

IV. CONCLUSION

Accordingly, for the reasons explained above, the Defendants' Motion for Reconsideration Under F.R.C.P. 59(e), ECF No. 67, is DENIED, and the Plaintiff's Motion to Strike the Declarations and Certain Exhibits Attached to Defendant's Motion for Reconsideration, ECF No. 68, is GRANTED. An appropriate Order will accompany this Memorandum Opinion.

DATED: January 3, 2013

Digitally signed by Beryl A. Howell
DN: cn=Beryl A. Howell, o=District Court for the District of Columbia, ou=United States District Court Judge, email=Howell_Chambers@dcd.uscourts.gov, c=US
Date: 2013.01.03 18:39:02 -05'00'

BERYL A. HOWELL
United States District Judge

US006081786A

United States Patent [19]

Barry et al.

[11] Patent Number: 6,081,786

[45] Date of Patent: Jun. 27, 2000

[54] **SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS**

[75] Inventors: **David W. Barry**, Chapel Hill; **Carolyn S. Underwood**, Cary; **Bruce J. McCreedy**, Raleigh; **David D. Hadden**, Durham, all of N.C.; **Jason L. Lucas**, West Chester, Pa.

[73] Assignee: **Triangle Pharmaceuticals, Inc.**, Durham, N.C.

[21] Appl. No.: **09/283,702**

[22] Filed: **Apr. 1, 1999**

Related U.S. Application Data

[60] Provisional application No. 60/080,629, Apr. 3, 1998.

[51] **Int. Cl.**[7] **G06F 17/60**

[52] **U.S. Cl.** **705/3**; 705/2; 706/45; 706/46; 706/47; 706/924

[58] **Field of Search** 705/3, 2, 1; 706/45, 706/10, 46, 47, 61, 924

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,839,822	6/1989	Dormond et al.	706/45
4,868,763	9/1989	Masui et al.	706/10
5,299,121	3/1994	Brill et al.	705/2
5,342,922	8/1994	Marshall et al.	530/329
5,355,444	10/1994	Chirico	706/45
5,517,405	5/1996	McAndrew	705/2
5,594,638	1/1997	Iliff	705/3
5,660,176	8/1997	Iliff	600/300
5,672,154	9/1997	Sillén et al.	604/505
5,694,950	12/1997	McMichael	128/898
5,737,539	4/1998	Edelson et al.	705/3
5,845,255	12/1998	Mayaud	705/3

(List continued on next page.)

OTHER PUBLICATIONS

Evans et al., *A Computer-Assisted Management Program for Antibiotics and Other Antiinfective Agents*, The N.E. Jour. of Med., vol. 338, No. 4, pp. 232–238 (Jan. 22, 1998).

Abstract, *Infectious Disease Alert*, Am. Health Consul., vol. 17, No. 11, pp. 81–82 (Mar. 1, 1998).

Pazzani et al., *Application of an Expert System in the Management of HIV-Infected Patients*, Jour. of Acq. Immune Def. Syndromes and Human Retrovirology, vol. 15, No. 5, pp. 356–362(1997).

Miller et al., *Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems*, Annals of Internal Medicine, vol. 127, No. 9, pp. 842–845 (Nov. 1, 1997).

Ziporyn, Terra, "Computer–Assisted Medical Decision–Making: Interest Growing", The Journal of the American Medical Association, pp. 913–918, Aug. 27, 1982.

Barnett, G. et al. "DXplain; An Evolving Diagnostic Decision–Support System", The Journal of the American Medical Association, pp. 67–74, Jul. 3, 1987.

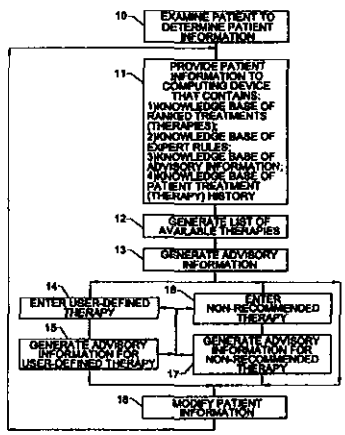
(List continued on next page.)

Primary Examiner—Emanuel Todd Voeltz
Assistant Examiner—John W. Hayes
Attorney, Agent, or Firm—Myers Bigel Sibley & Sajovec

[57] **ABSTRACT**

Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen for a known disease such as HIV infection are disclosed. The method comprises (a) providing patient information to a computing device (the computer device comprising: a first knowledge base comprising a plurality of different therapeutic treatment regimens for the disease; a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for the disease; and a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of the different therapeutic treatment regimens; and (b) generating in the computing device a listing (preferably a ranked listing) of therapeutic treatment regimens for the patient; and (c) generating in the computing device advisory information for one or more treatment regimens in the listing based on the patient information and the expert rules.

66 Claims, 22 Drawing Sheets



U.S. PATENT DOCUMENTS

5,908,383	6/1999	Brynjestand	600/300
5,911,132	6/1999	Sloane	705/3
5,924,074	7/1999	Evans	705/3
5,950,630	9/1999	Portwood et al.	705/3

OTHER PUBLICATIONS

Wyatt, Jeremy, "Computer-based Knowledge Systems", Lancet, vol. 338, No. 8780, pp. 1431-1437, Dec. 7, 1991.

"UCSF Launches Website 'HIV InSite', A Comprehensive Online gateway to AIDS Knowledge", Business Wire, Dialog File 148:Trade & Industry Database, Mar. 17, 1997.

Evans et al, "A Computer-Assisted Management Program for Antibiotics and Other Antiinfective Agents", The New England Journal of Medicine, vol. 338, No. 4, pp. 232-238, Jan. 22, 1998.

Abstract, "Infectious Disease Alert", American Health Consultants, vol. 17, No. 11, pp. 81-82, Mar. 1, 1998.

Pazzani et al, "Application of an Expert System in the Management of HIV-Infected Patients", Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, vol. 15, No. 5, pp. 356-362, 1997.

Miller et al, Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems, Annals of Internal Medicine, vol. 127, No. 9, pp. 842-845, Nov. 1, 1997.

International Search Report, PCT Application No. PCT/US99/07171 (Oct. 22, 1999).

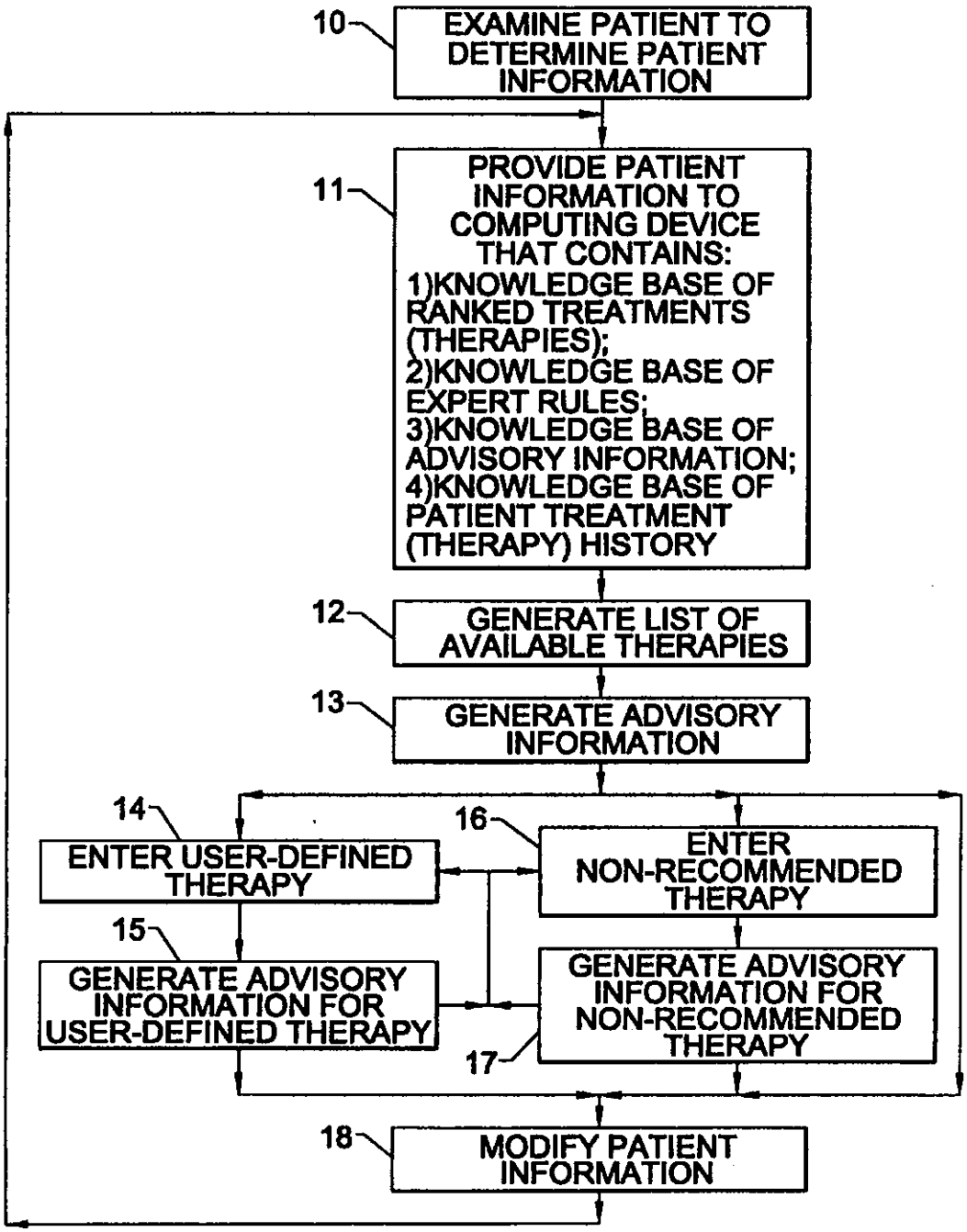

10
EXAMINE PATIENT TO DETERMINE PATIENT INFORMATION
11
PROVIDE PATIENT INFORMATION TO COMPUTING DEVICE THAT CONTAINS:
1)KNOWLEDGE BASE OF RANKED TREATMENTS (THERAPIES);
2)KNOWLEDGE BASE OF EXPERT RULES;
3)KNOWLEDGE BASE OF ADVISORY INFORMATION;
4)KNOWLEDGE BASE OF PATIENT TREATMENT (THERAPY) HISTORY
12
GENERATE LIST OF AVAILABLE THERAPIES
13
GENERATE ADVISORY INFORMATION
14
ENTER USER-DEFINED THERAPY
16
ENTER NON-RECOMMENDED THERAPY
15
GENERATE ADVISORY INFORMATION FOR USER-DEFINED THERAPY
GENERATE ADVISORY INFORMATION FOR NON-RECOMMENDED THERAPY
17
18
MODIFY PATIENT INFORMATION

FIG. 1.

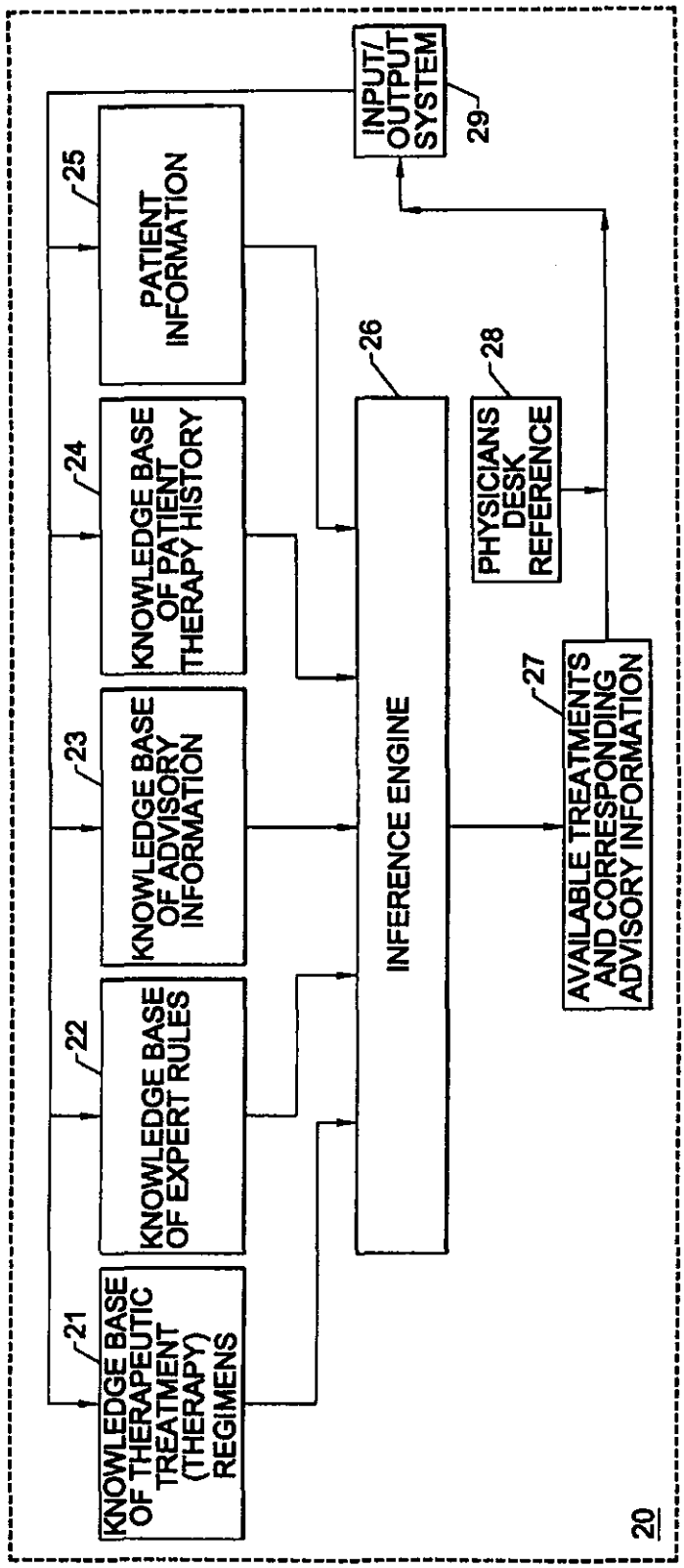


FIG. 2.

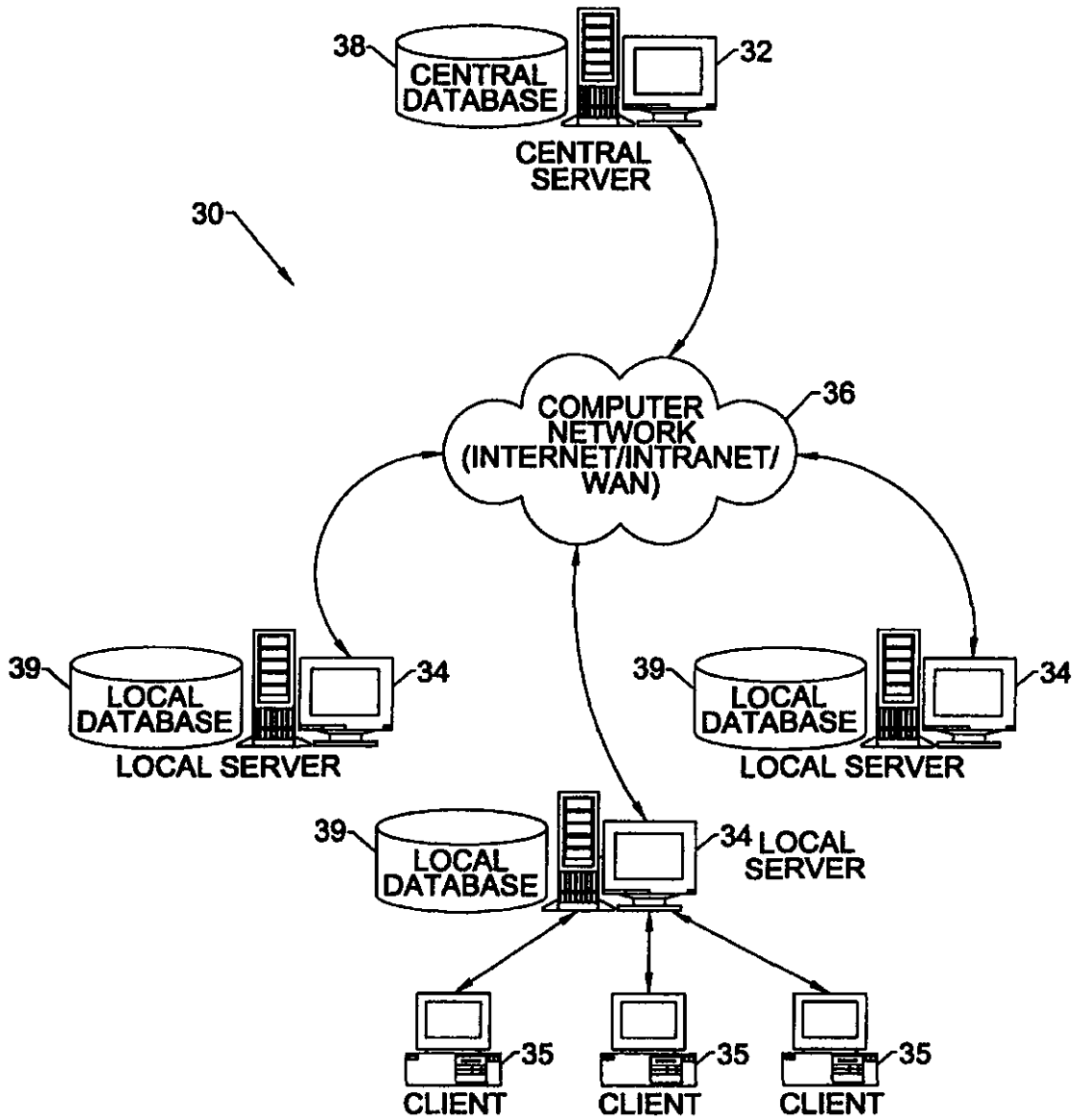

38
CENTRAL DATABASE
32
CENTRAL SERVER
30
COMPUTER NETWORK (INTERNET/INTRANET/ WAN)
36
39
LOCAL DATABASE
34
LOCAL SERVER
39
LOCAL DATABASE
34
LOCAL SERVER
39
LOCAL DATABASE
34 LOCAL SERVER
35
CLIENT
35
CLIENT
35
CLIENT

FIG. 3.

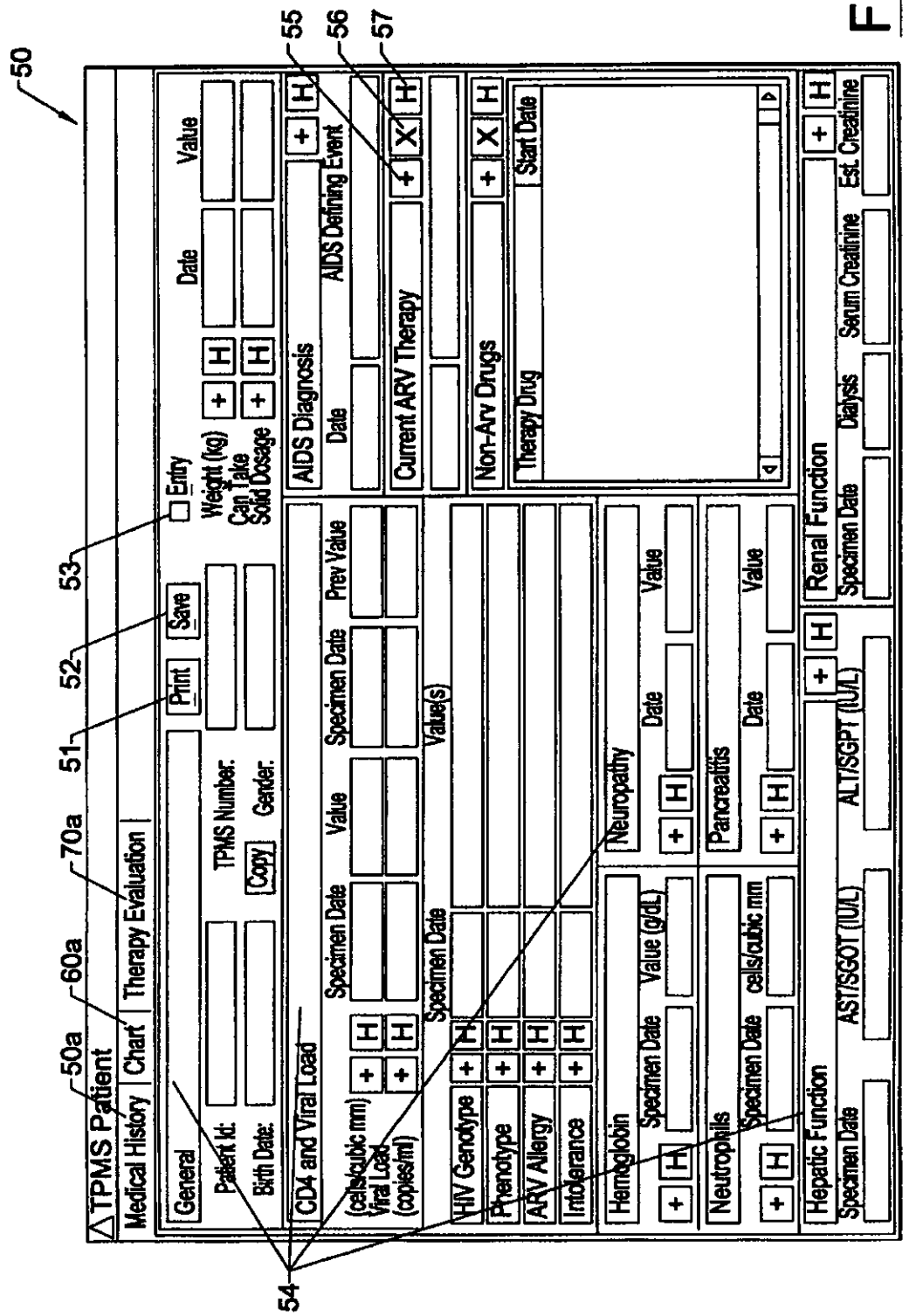


FIG. 4.

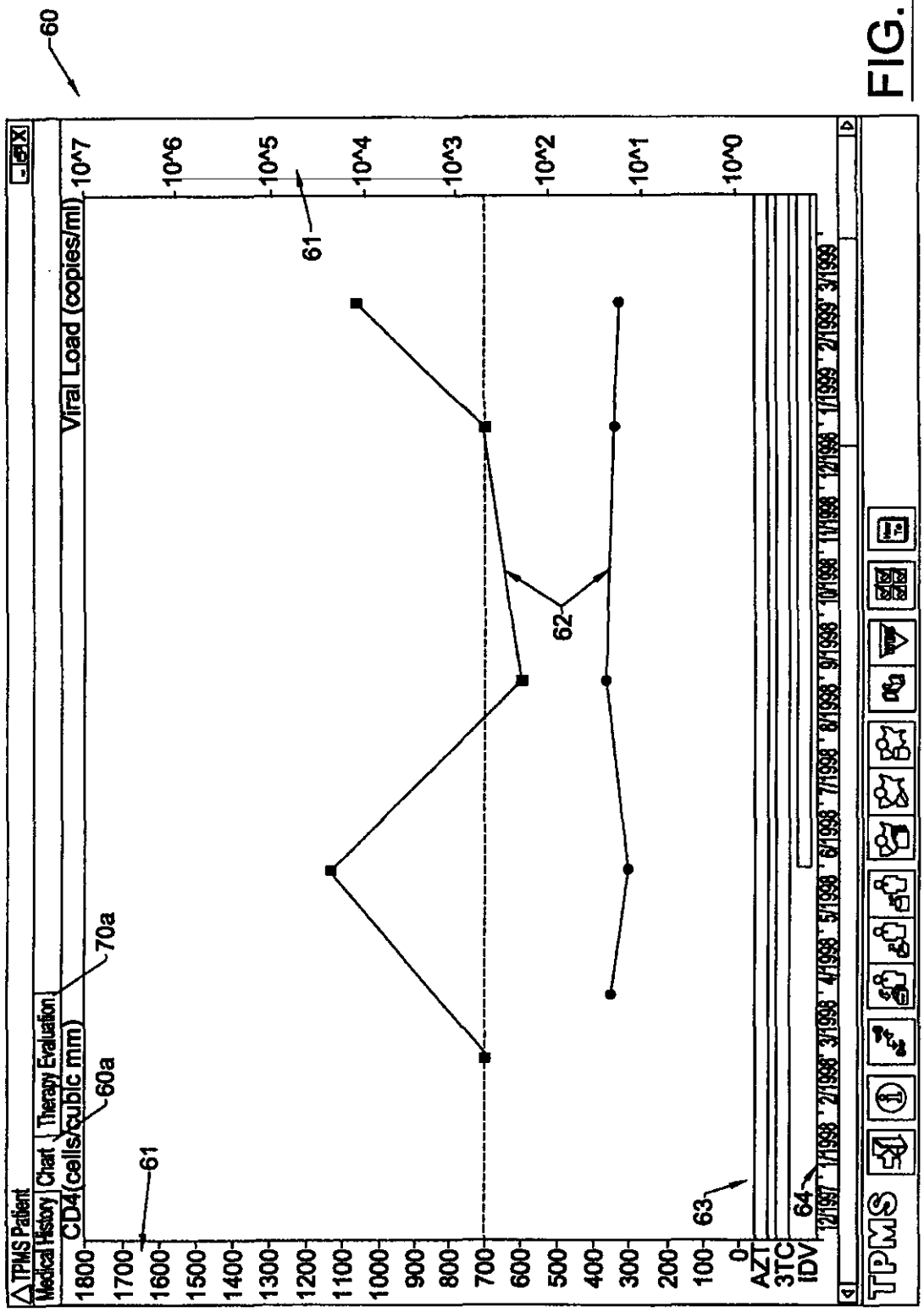
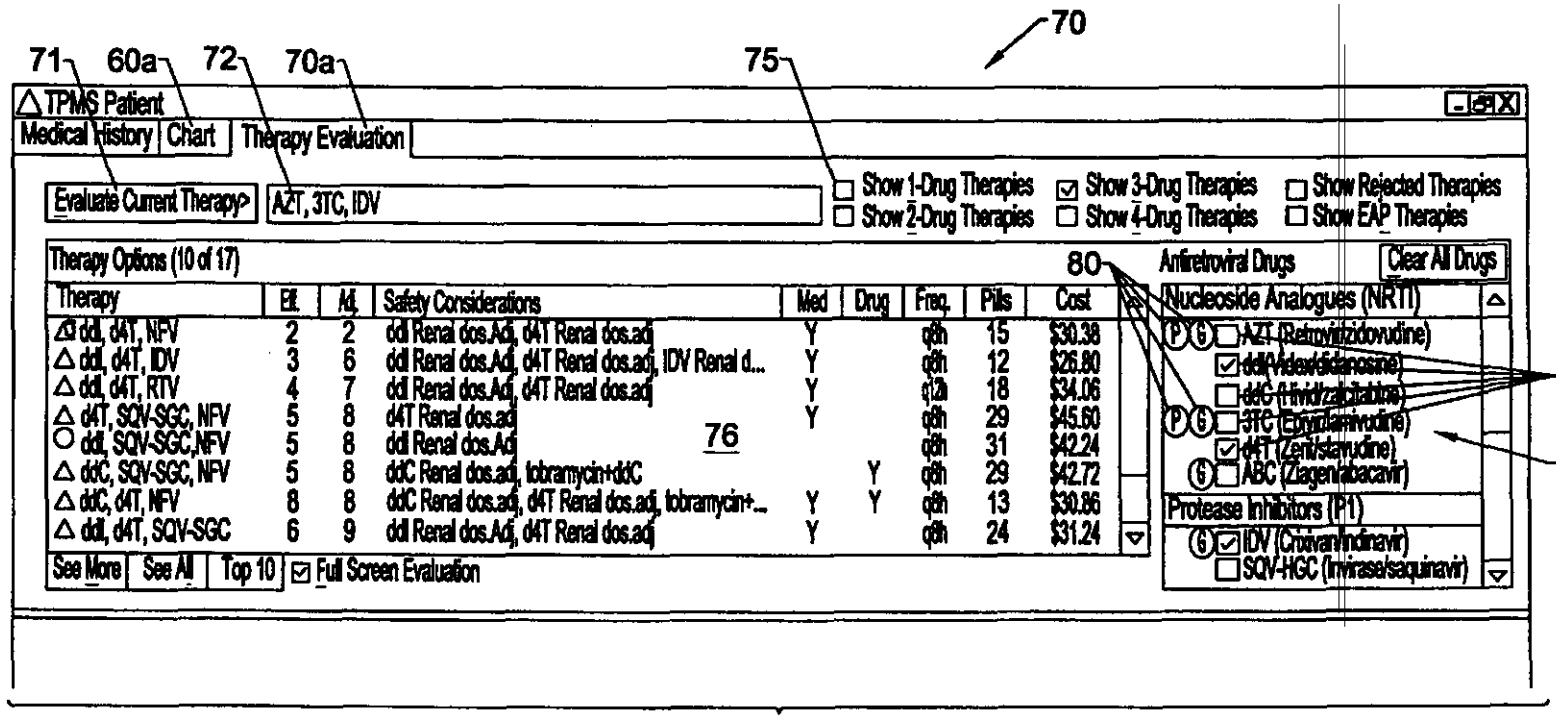


FIG. 5.



TO FIG. 6B.

FIG. 6A.

A 72

FROM FIG. 6A.

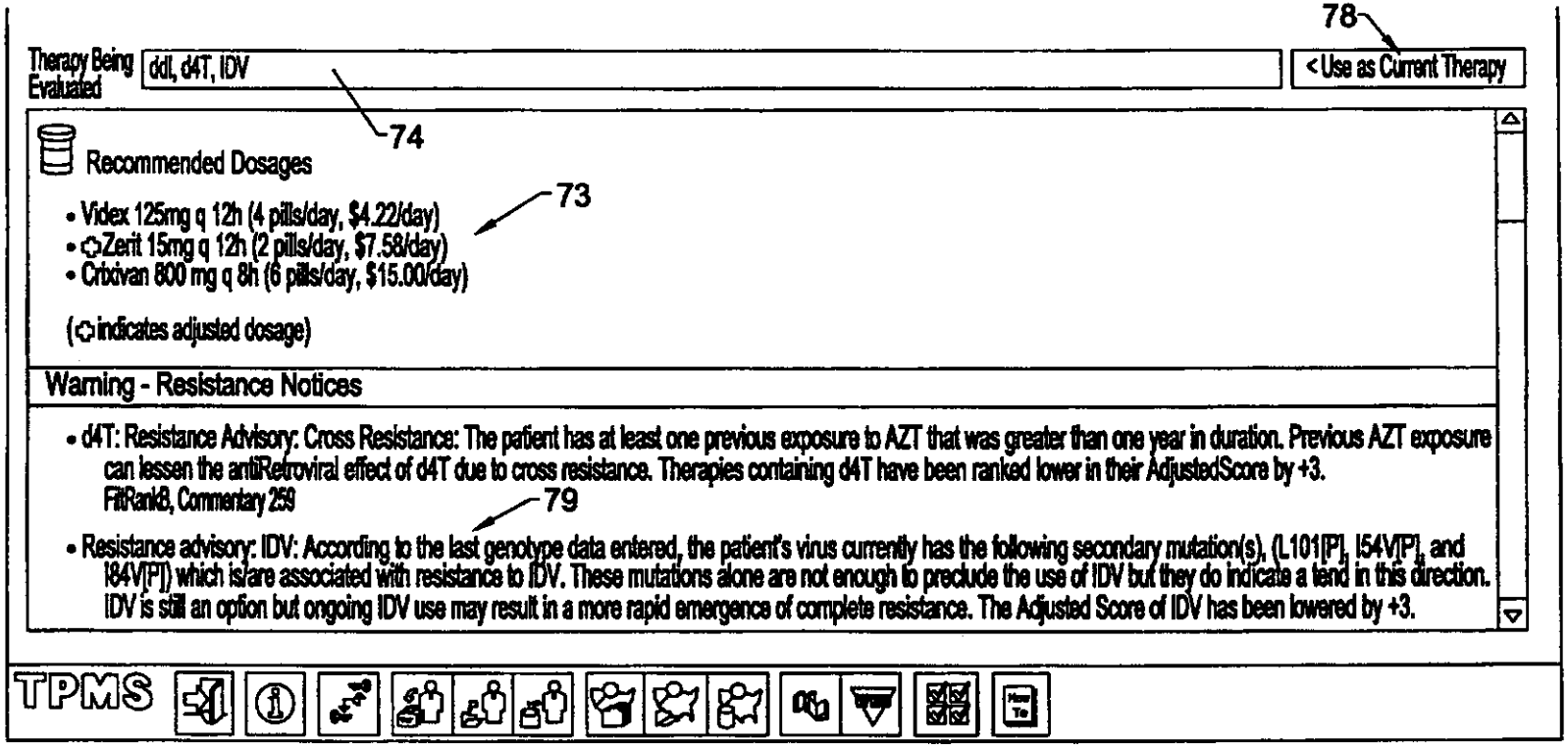


FIG. 6B.

Icon	Meaning
○	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box.
◎	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box. The book indicates that therapy has been studied and a reference is available to review.
△	Indicates a yellow alert. There is important information about this therapy that must be reviewed.
◭	Indicates a yellow alert. There is important information about this therapy that must be reviewed. The book indicates that therapy has been studied and a reference is available to review.
!	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this therapy to be considered.
!◎	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this thereapy to be considered. The book indicates that therapy has been studied and a reference is available to review.
X	Indicates the therapy is not recommended.

FIG. 7.

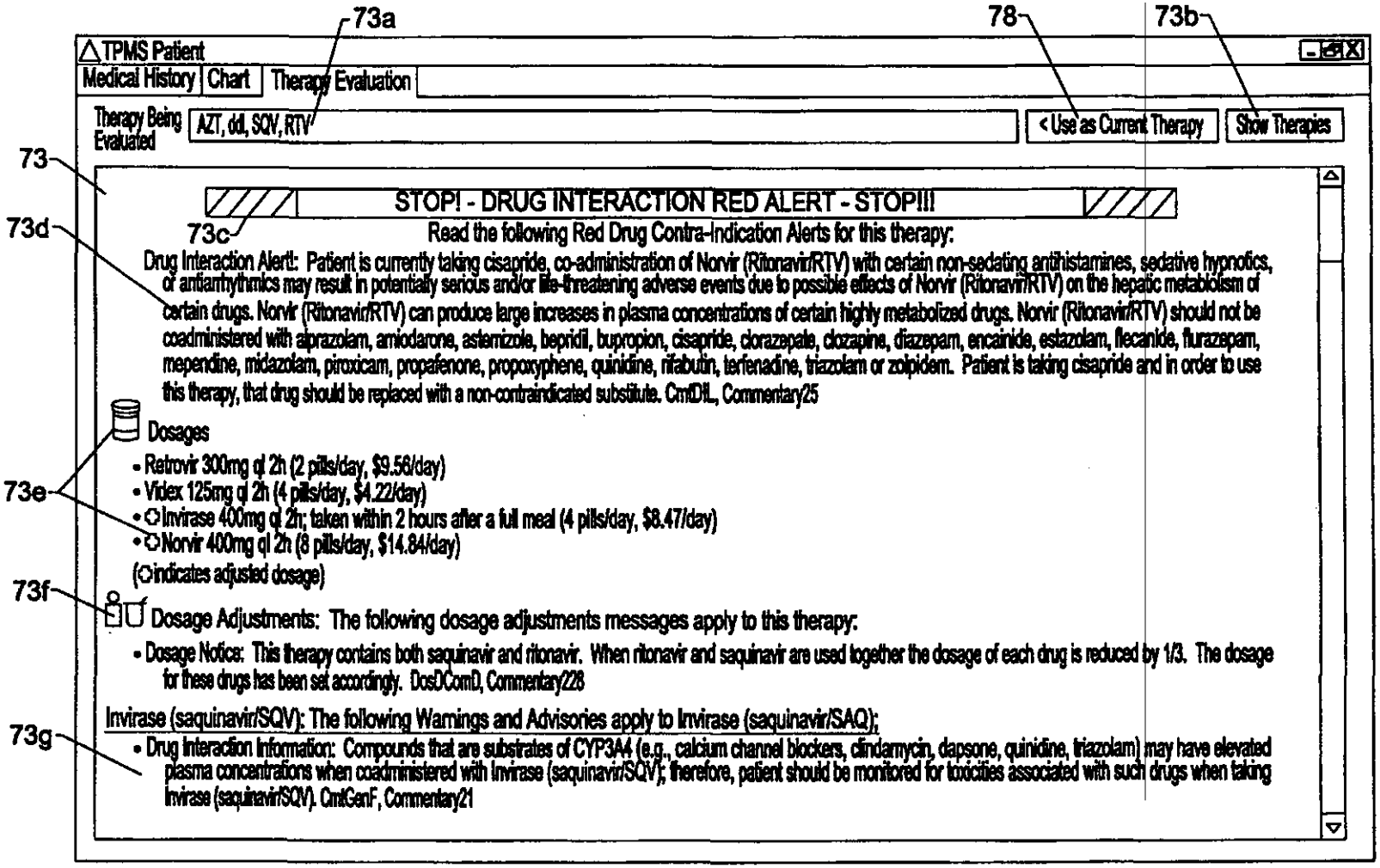

73a
78
73b
TPMS Patient
Medical History
Chart
Therapy Evaluation
Therapy Being Evaluated
AZT, dd, SQV, RTV
< Use as Current Therapy
Show Therapies
73
73d
STOP! - DRUG INTERACTION RED ALERT - STOP!!!
73c
Read the following Red Drug Contra-Indication Alerts for this therapy:
Drug Interaction Alert!: Patient is currently taking cisapride, co-administration of Norvir (Ritonavir/RTV) with certain non-sedating antihistamines, sedative hypnotics, or antiarrhythmics may result in potentially serious and/or life-threatening adverse events due to possible effects of Norvir (Ritonavir/RTV) on the hepatic metabolism of certain drugs. Norvir (Ritonavir/RTV) can produce large increases in plasma concentrations of certain highly metabolized drugs. Norvir (Ritonavir/RTV) should not be coadministered with alprazolam, amiodarone, astemizole, bepridil, bupropion, cisapride, clorazepate, clozapine, diazepam, encainide, estazolam, flecanide, flurazepam, mependine, midazolam, piroxicam, propafenone, propoxyphene, quinidine, rifabutin, terfenadine, triazolam or zolpidem. Patient is taking cisapride and in order to use this therapy, that drug should be replaced with a non-contraindicated substitute. CmtDIL, Commentary25
Dosages
73e
• Retrovir 300mg ql 2h (2 pills/day, $9.56/day)
• Videx 125mg ql 2h (4 pills/day, $4.22/day)
• ○Invirase 400mg ql 2h; taken within 2 hours after a full meal (4 pills/day, $8.47/day)
• ○Norvir 400mg ql 2h (8 pills/day, $14.84/day)
(○indicates adjusted dosage)
73f
Dosage Adjustments: The following dosage adjustments messages apply to this therapy:
• Dosage Notice: This therapy contains both saquinavir and ritonavir. When ritonavir and saquinavir are used together the dosage of each drug is reduced by 1/3. The dosage for these drugs has been set accordingly. DosDComD, Commentary228
Invirase (saquinavir/SQV): The following Warnings and Advisories apply to Invirase (saquinavir/SAQ):
73g
• Drug Interaction Information: Compounds that are substrates of CYP3A4 (e.g., calcium channel blockers, clindamycin, dapsone, quinidine, triazolam) may have elevated plasma concentrations when coadministered with Invirase (saquinavir/SQV); therefore, patient should be monitored for toxicities associated with such drugs when taking Invirase (saquinavir/SQV). CmtGenF, Commentary21

FIG. 8.

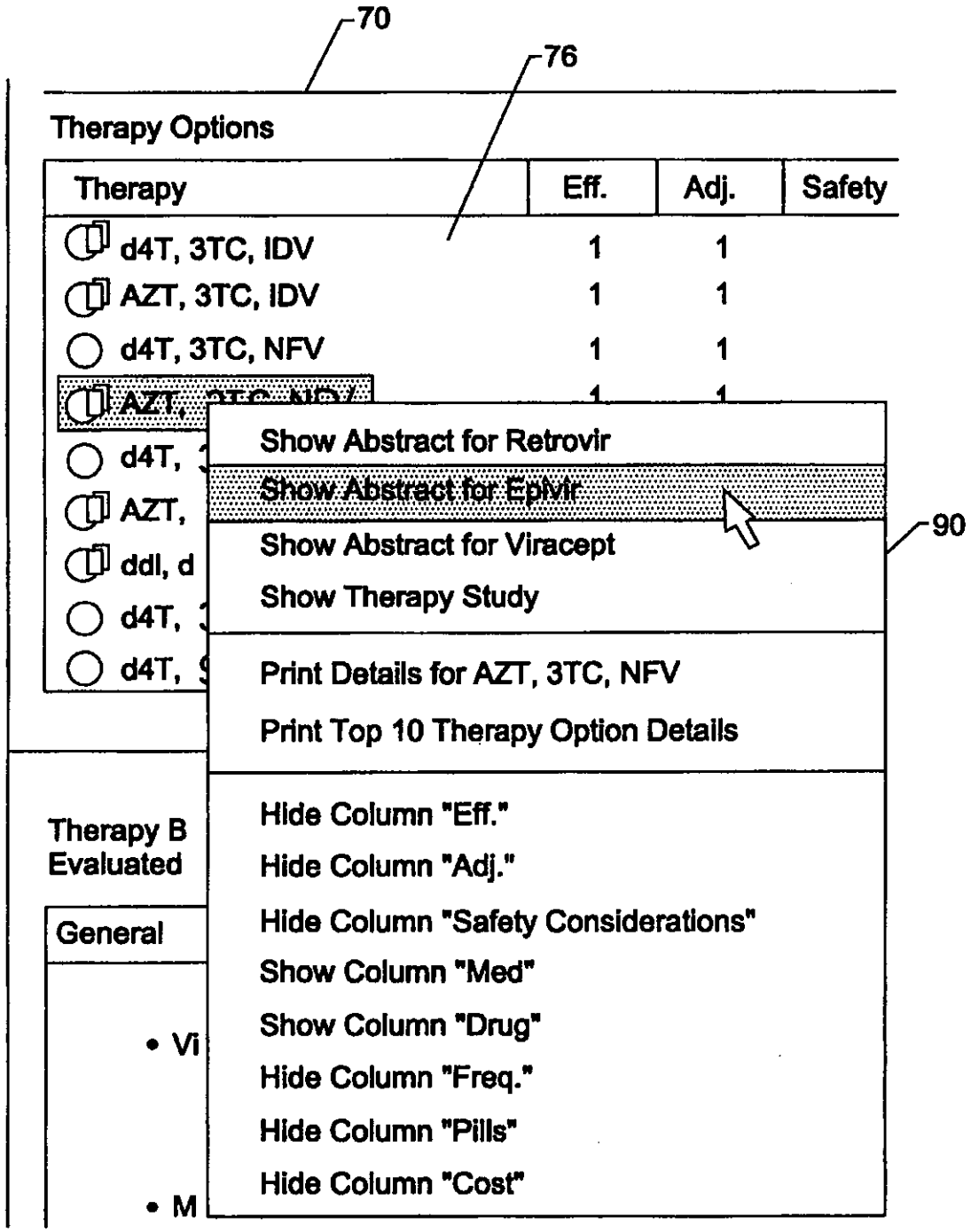

70
76
Therapy Options
Therapy
Eff.
Adj.
Safety
d4T, 3TC, IDV 1 1
AZT, 3TC, IDV 1 1
d4T, 3TC, NFV 1 1
Show Abstract for Retrovir
Show Abstract for Epivir
Show Abstract for Viracept
Show Therapy Study
Print Details for AZT, 3TC, NFV
Print Top 10 Therapy Option Details
Hide Column "Eff."
Hide Column "Adj."
Hide Column "Safety Considerations"
Show Column "Med"
Show Column "Drug"
Hide Column "Freq."
Hide Column "Pills"
Hide Column "Cost"
90
Therapy B
Evaluated
General

FIG. 9.

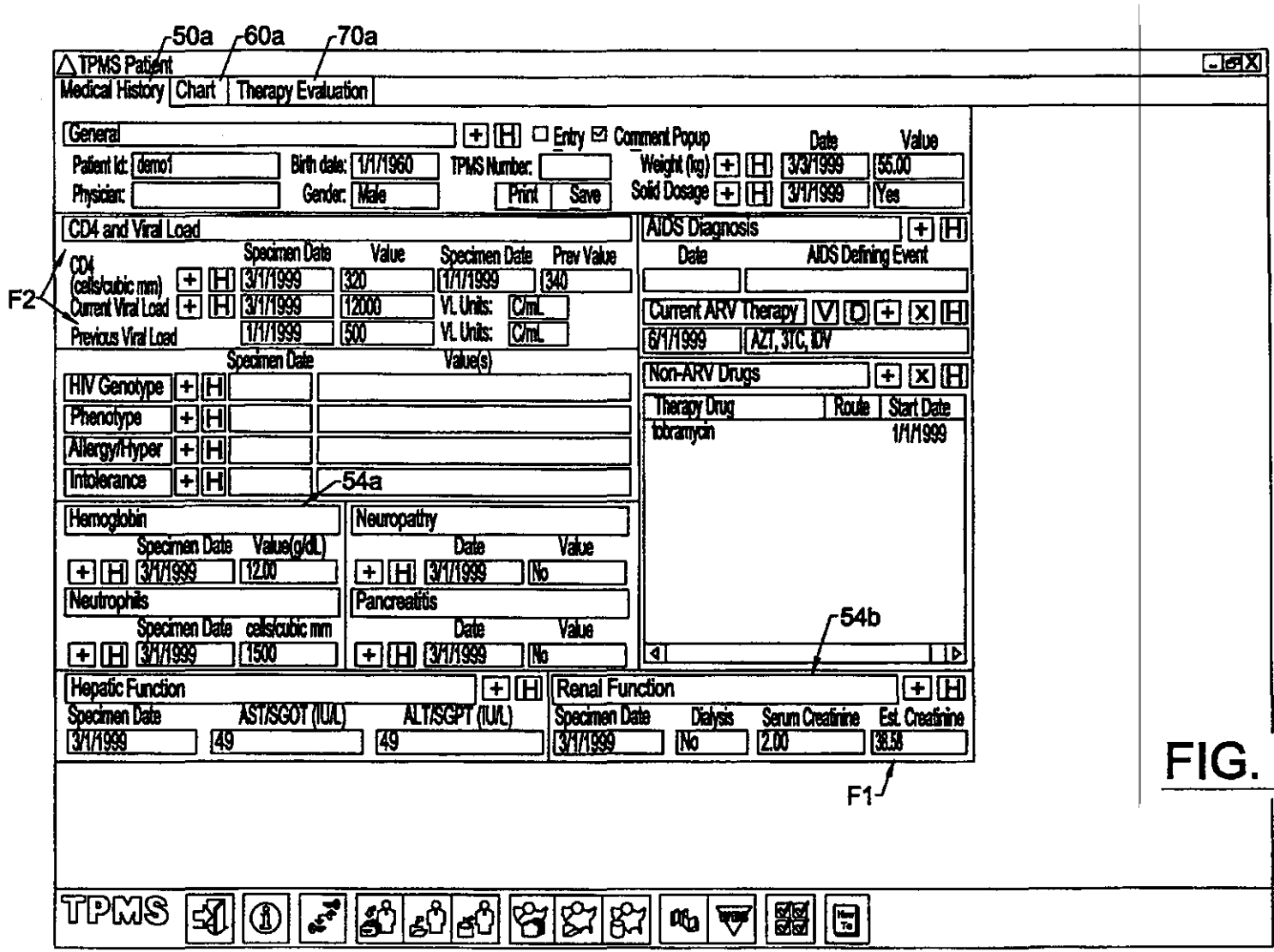

50a
60a
70a
50
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Patient Id: demo1
Birth date: 1/1/1950
TPMS Number:
Physician:
Gender: Male
Print
Save
Weight (kg) 3/3/1999 55.00
Solid Dosage 3/1/1999 Yes
CD4 and Viral Load
CD4 (cells/cubic mm) 3/1/1999 320 1/1/1999 340
Current Viral Load 3/1/1999 12000 VL Units: C/mL
Previous Viral Load 1/1/1999 500 VL Units: C/mL
F2
AIDS Diagnosis
Date
AIDS Defining Event
Current ARV Therapy
6/1/1999 AZT, 3TC, IDV
Non-ARV Drugs
Therapy Drug
Route
Start Date
Tobramycin 1/1/1999
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
54a
Hemoglobin
Specimen Date
Value(g/dL)
3/1/1999 12.00
Neuropathy
Date
Value
3/1/1999 No
Neutrophils
Specimen Date
cells/cubic mm
3/1/1999 1500
Pancreatitis
Date
Value
3/1/1999 No
54b
Hepatic Function
Specimen Date
AST/SGOT (IU/L)
ALT/SGPT (IU/L)
3/1/1999 49 49
Renal Function
Specimen Date
Dialysis
Serum Creatinine
Est. Creatinine
3/1/1999 No 2.00 38.58
F1
TPMS

FIG. 10A.

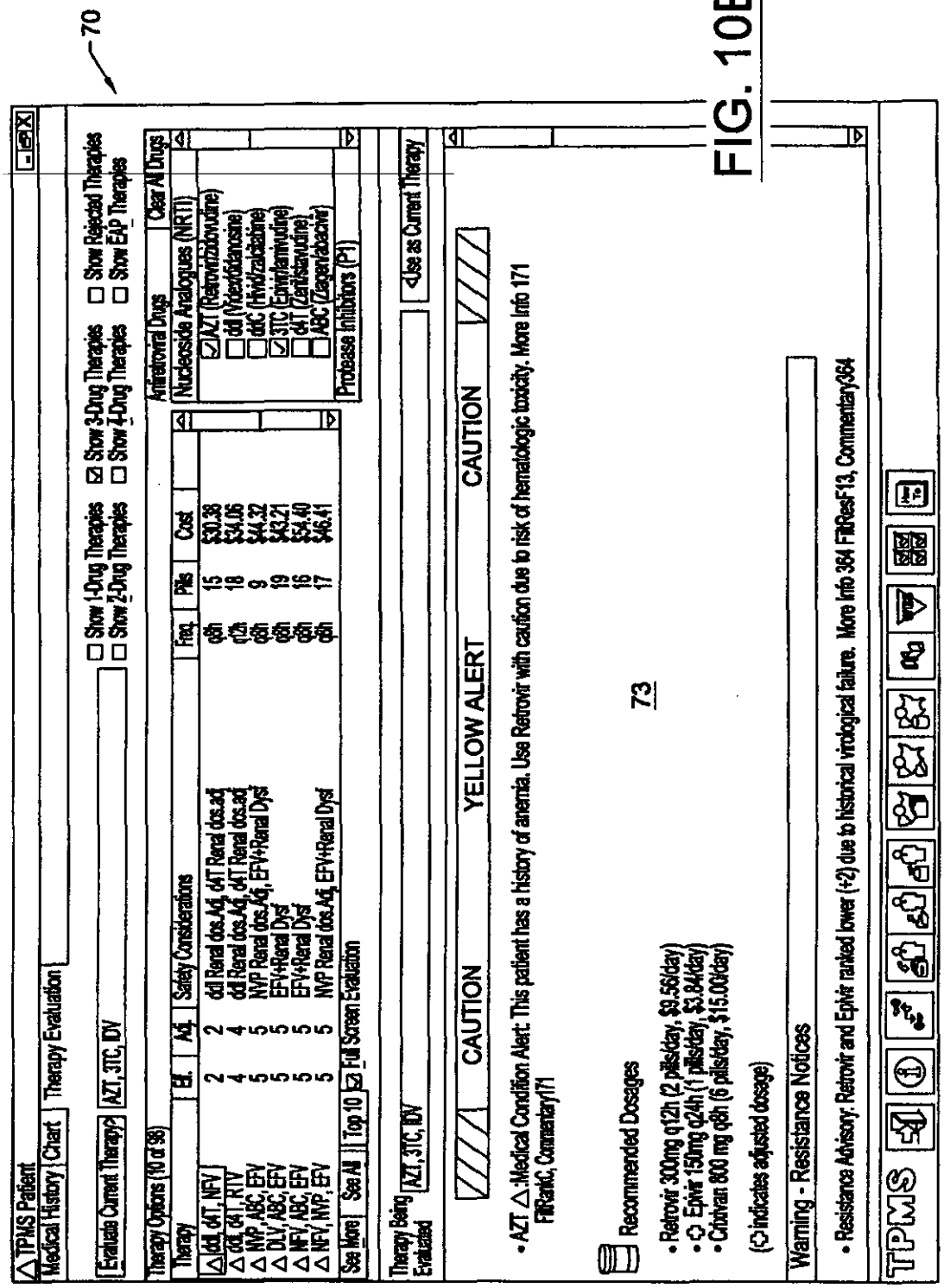


FIG. 10B.

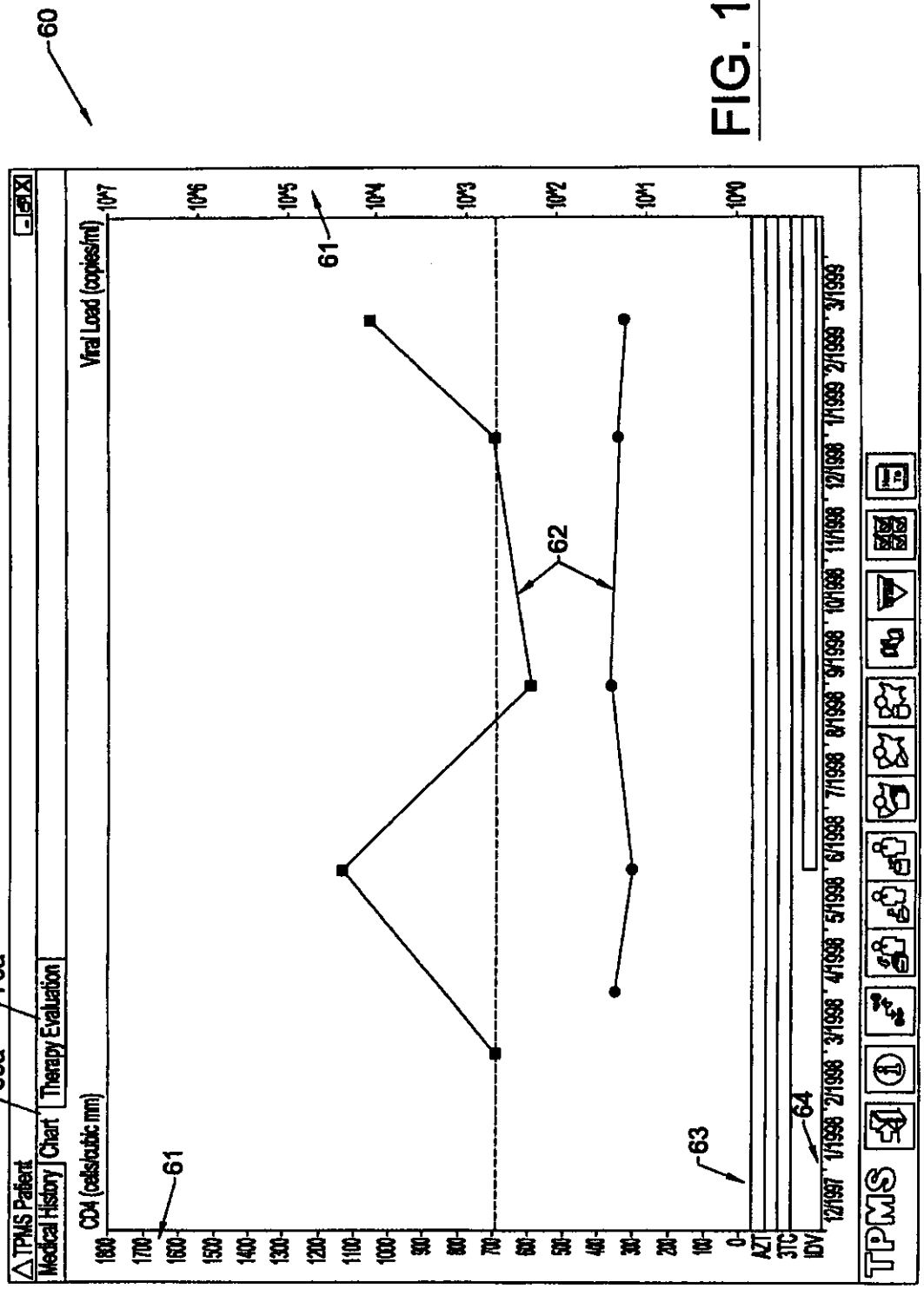

60
60a
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
CD4 (cells/cubic mm)
Viral Load (copies/ml)
61
62
63
64
AZT
3TC
IDV
TPMS

FIG. 10C.

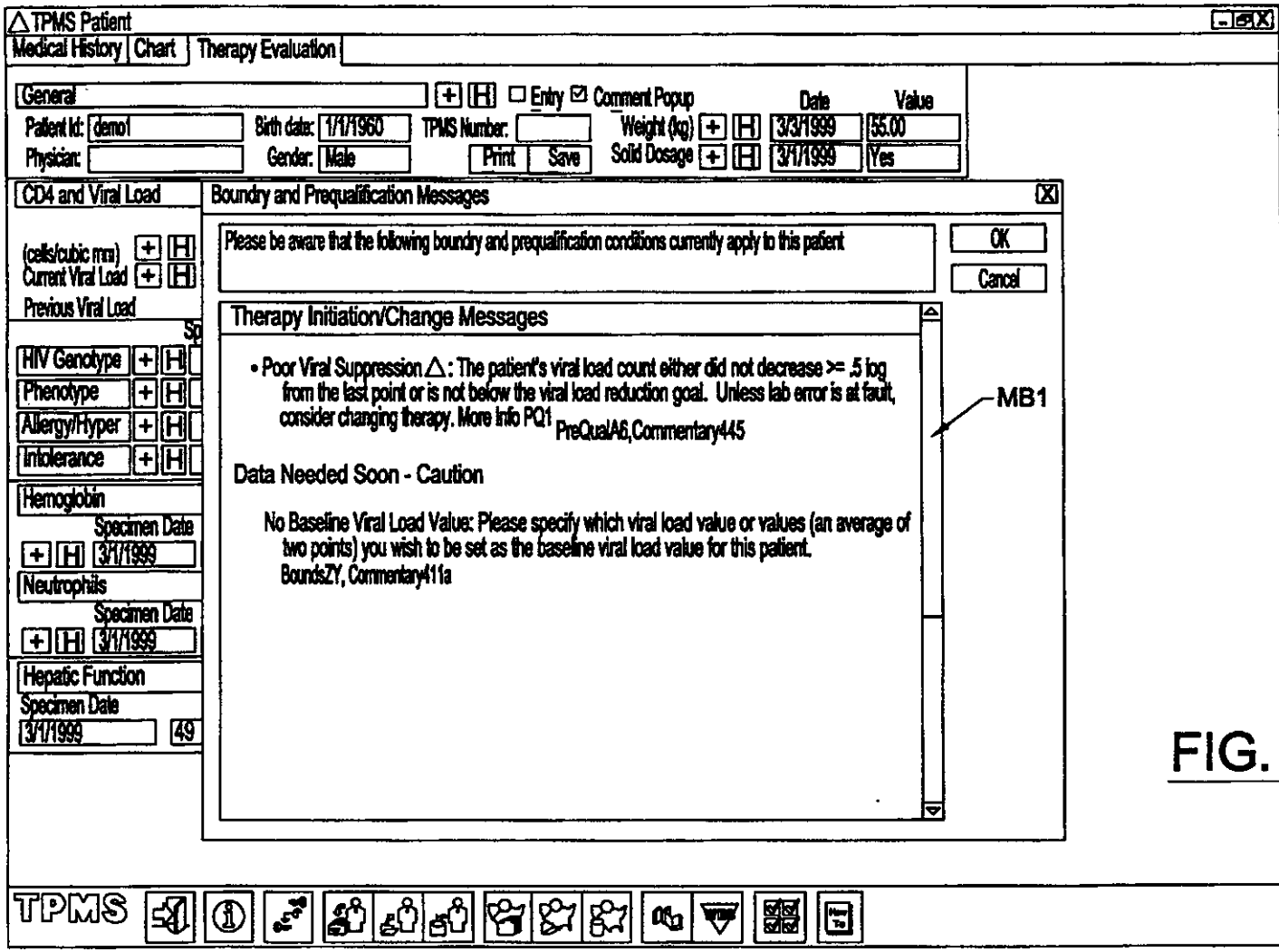

TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Date
Value
Patient Id: demo1
Birth date: 1/1/1960
TPMS Number:
Weight (kg)
3/3/1999
55.00
Physician:
Gender: Male
Print
Save
Solid Dosage
3/1/1999
Yes
CD4 and Viral Load
(cells/cubic mm)
Current Viral Load
Previous Viral Load
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Hemoglobin
Specimen Date
3/1/1999
Neutrophils
Specimen Date
3/1/1999
Hepatic Function
Specimen Date
3/1/1999
49
Boundry and Prequalification Messages
Please be aware that the following boundry and prequalification conditions currently apply to this patient
OK
Cancel
Therapy Initiation/Change Messages
• Poor Viral Suppression △: The patient's viral load count either did not decrease >= .5 log from the last point or is not below the viral load reduction goal. Unless lab error is at fault, consider changing therapy. More Info PQ1 PreQualA6,Commentary445
Data Needed Soon - Caution
No Baseline Viral Load Value: Please specify which viral load value or values (an average of two points) you wish to be set as the baseline viral load value for this patient. BoundsZY, Commentary411a
MB1
TPMS
70

FIG. 10D.

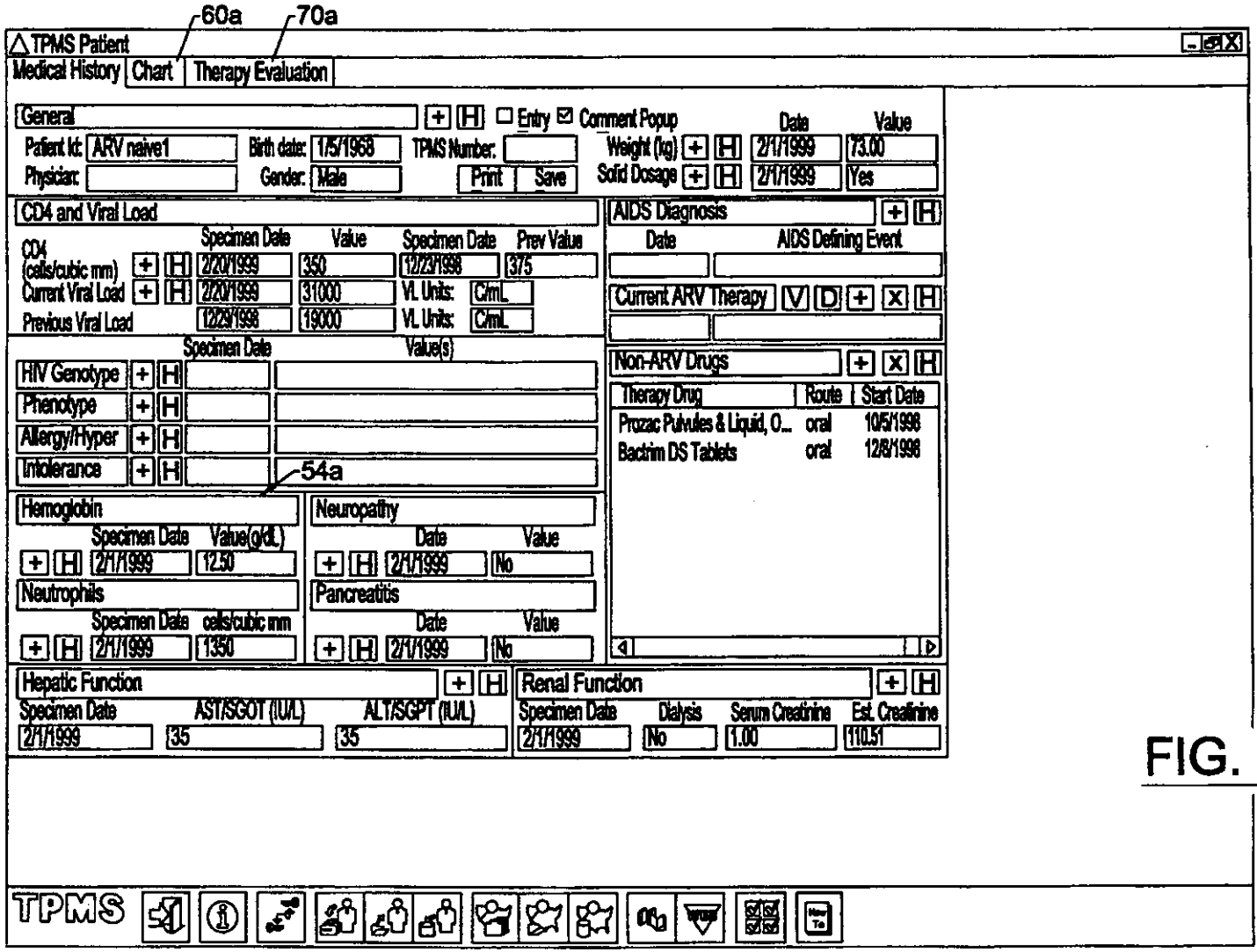

60a
70a
50
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Patient Id: ARV naive1
Birth date: 1/5/1968
TPMS Number:
Physician:
Gender: Male
Print
Save
Weight (kg) 2/1/1999 73.00
Solid Dosage 2/1/1999 Yes
CD4 and Viral Load
Specimen Date
Value
Prev Value
CD4 (cells/cubic mm) 2/20/1999 350 12/23/1998 375
Current Viral Load 2/20/1999 31000 VL Units: C/mL
Previous Viral Load 12/29/1998 19000 VL Units: C/mL
AIDS Diagnosis
Date
AIDS Defining Event
Current ARV Therapy
Non-ARV Drugs
Therapy Drug
Route
Start Date
Prozac Pulvules & Liquid, O... oral 10/5/1998
Bactrim DS Tablets oral 12/8/1998
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Value(s)
54a
Hemoglobin
Specimen Date
Value(g/dL)
2/1/1999 12.50
Neuropathy
Date
Value
2/1/1999 No
Neutrophils
Specimen Date
cells/cubic mm
2/1/1999 1350
Pancreatitis
Date
Value
2/1/1999 No
Hepatic Function
Specimen Date
AST/SGOT (IU/L)
ALT/SGPT (IU/L)
2/1/1999 35 35
Renal Function
Specimen Date
Dialysis
Serum Creatinine
Est. Creatinine
2/1/1999 No 1.00 110.51
TPMS

FIG. 11A.

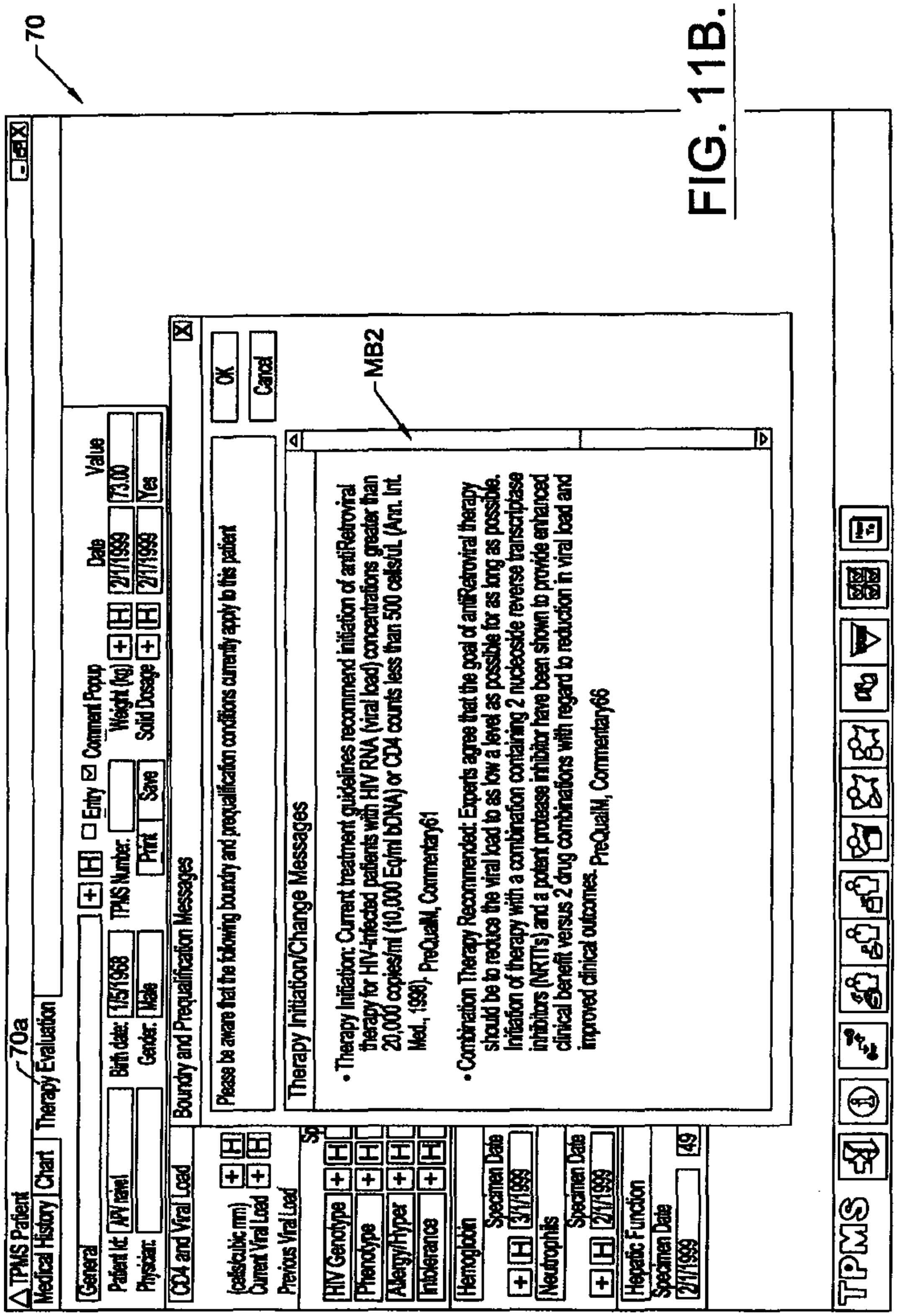

70
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Patient Id: APVnaivel
Physician:
Birth date: 1/5/1968
Gender: Male
TPMS Number:
Entry
Comment Popup
Weight (kg)
Solid Dosage
Date
Value
2/1/1999
73.00
Yes
Print
Save
CD4 and Viral Load
(cells/cubic mm)
Current Viral Load
Previous Viral Load
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Hemoglobin
Specimen Date
3/1/1999
Neutrophils
Specimen Date
2/1/1999
Hepatic Function
Specimen Date
2/1/1999
49
Boundry and Prequalification Messages
Please be aware that the following boundry and prequalification conditions currently apply to this patient
OK
Cancel
MB2
Therapy Initiation/Change Messages
• Therapy Initiation: Current treatment guidelines recommend initiation of antiRetroviral therapy for HIV-infected patients with HIV RNA (viral load) concentrations greater than 20,000 copies/ml (10,000 Eq/ml bDNA) or CD4 counts less than 500 cells/uL (Ann. Int. Med., 1998). PreQualM, Commentary61
• Combination Therapy Recommended: Experts agree that the goal of antiRetroviral therapy should be to reduce the viral load to as low a level as possible for as long as possible. Initiation of therapy with a combination containing 2 nucleoside reverse transcriptase inhibitors (NRTI's) and a potent protease inhibitor have been shown to provide enhanced clinical benefit versus 2 drug combinations with regard to reduction in viral load and improved clinical outcomes. PreQualM, Commentary66
TPMS

FIG. 11B.

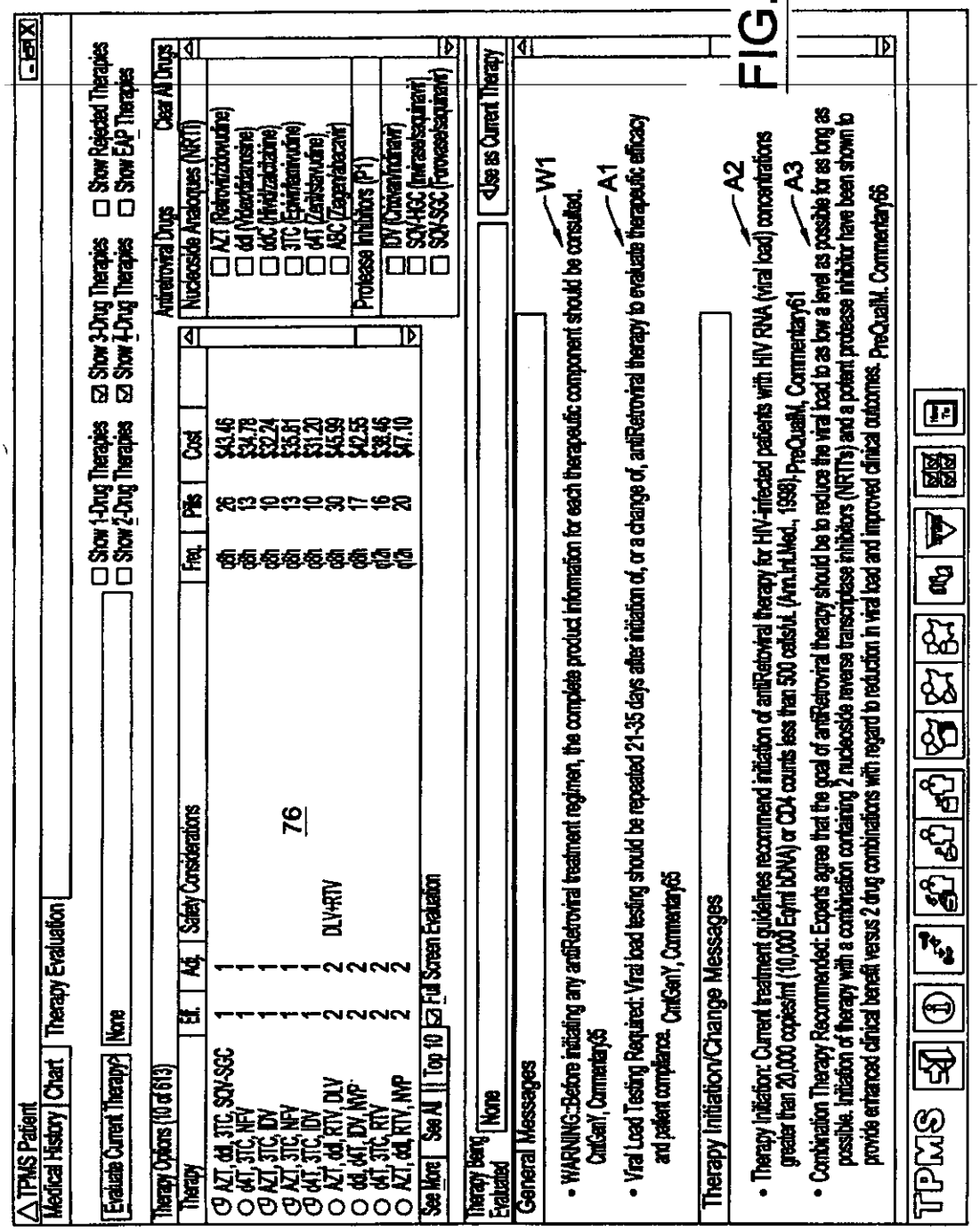


FIG. 11C.

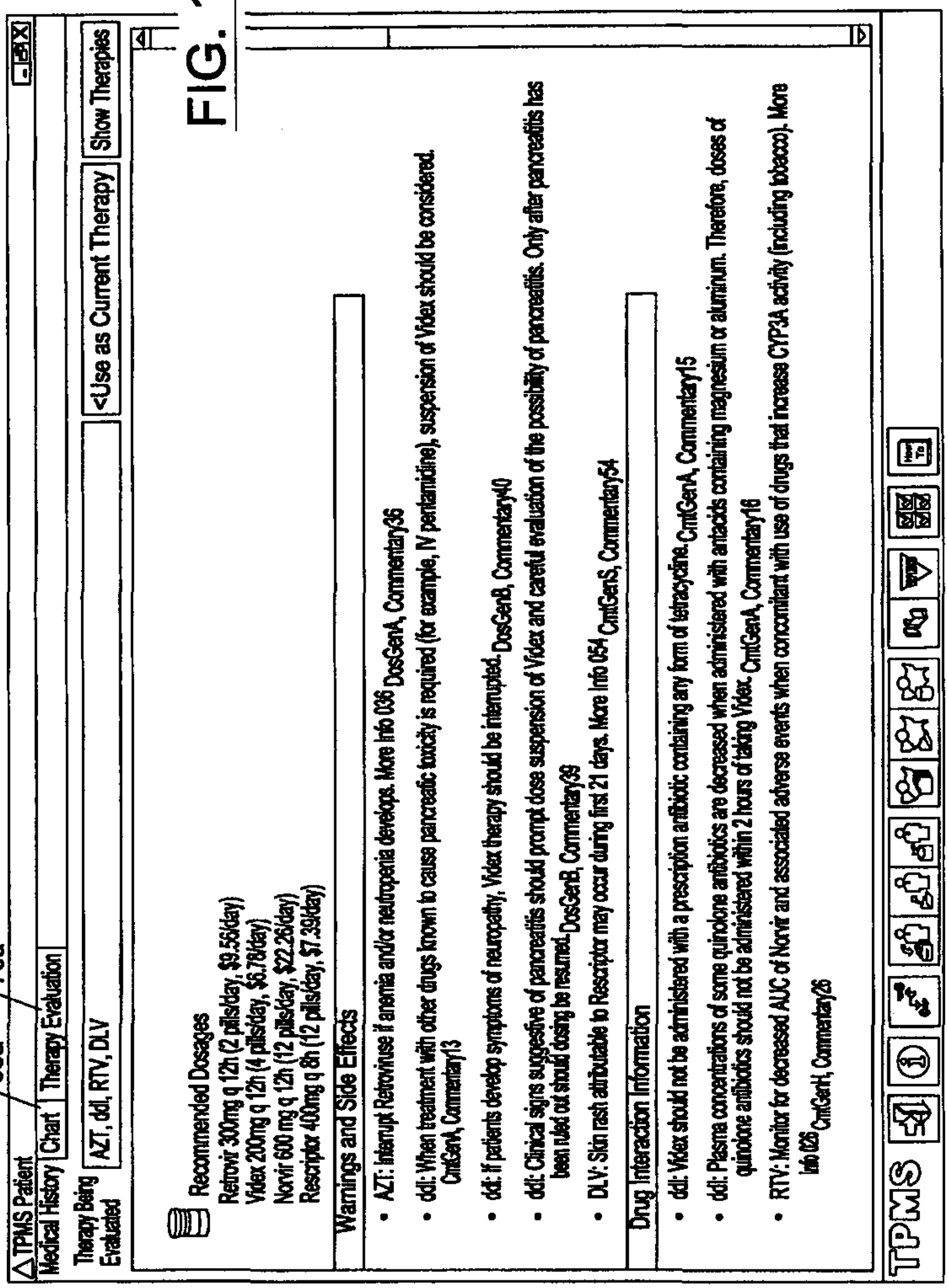

60a
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
Therapy Being Evaluated
AZT, ddI, RTV, DLV
<Use as Current Therapy
Show Therapies
Recommended Dosages
Retrovir 300mg q 12h (2 pills/day, $9.55/day)
Videx 200mg q 12h (4 pills/day, $6.78/day)
Norvir 600 mg q 12h (12 pills/day, $22.26/day)
Rescriptor 400mg q 8h (12 pills/day, $7.39/day)
Warnings and Side Effects
• AZT: Interrupt Retrovirus if anemia and/or neutropenia develops. More Info 036 DosGenA, Commentary36
• ddI: When treatment with other drugs known to cause pancreatic toxicity is required (for example, IV pentamidine), suspension of Videx should be considered. CmtGenA, Commentary13
• ddI: If patients develop symptoms of neuropathy, Videx therapy should be interrupted. DosGenB, Commentary40
• ddI: Clinical signs suggestive of pancreatitis should prompt dose suspension of Videx and careful evaluation of the possibility of pancreatitis. Only after pancreatitis has been ruled out should dosing be resumed. DosGenB, Commentary39
• DLV: Skin rash attributable to Rescriptor may occur during first 21 days. More Info 054 CmtGenS, Commentary54
Drug Interaction Information
• ddI: Videx should not be administered with a prescription antibiotic containing any form of tetracycline. CmtGenA, Commentary15
• ddI: Plasma concentrations of some quinolone antibiotics are decreased when administered with antacids containing magnesium or aluminum. Therefore, doses of quinolone antibiotics should not be administered within 2 hours of taking Videx. CmtGenA, Commentary16
• RTV: Monitor for decreased AUC of Norvir and associated adverse events when concomitant with use of drugs that increase CYP3A activity (including tobacco). More Info 026 CmtGenH, Commentary26
TPMS

FIG. 11D.

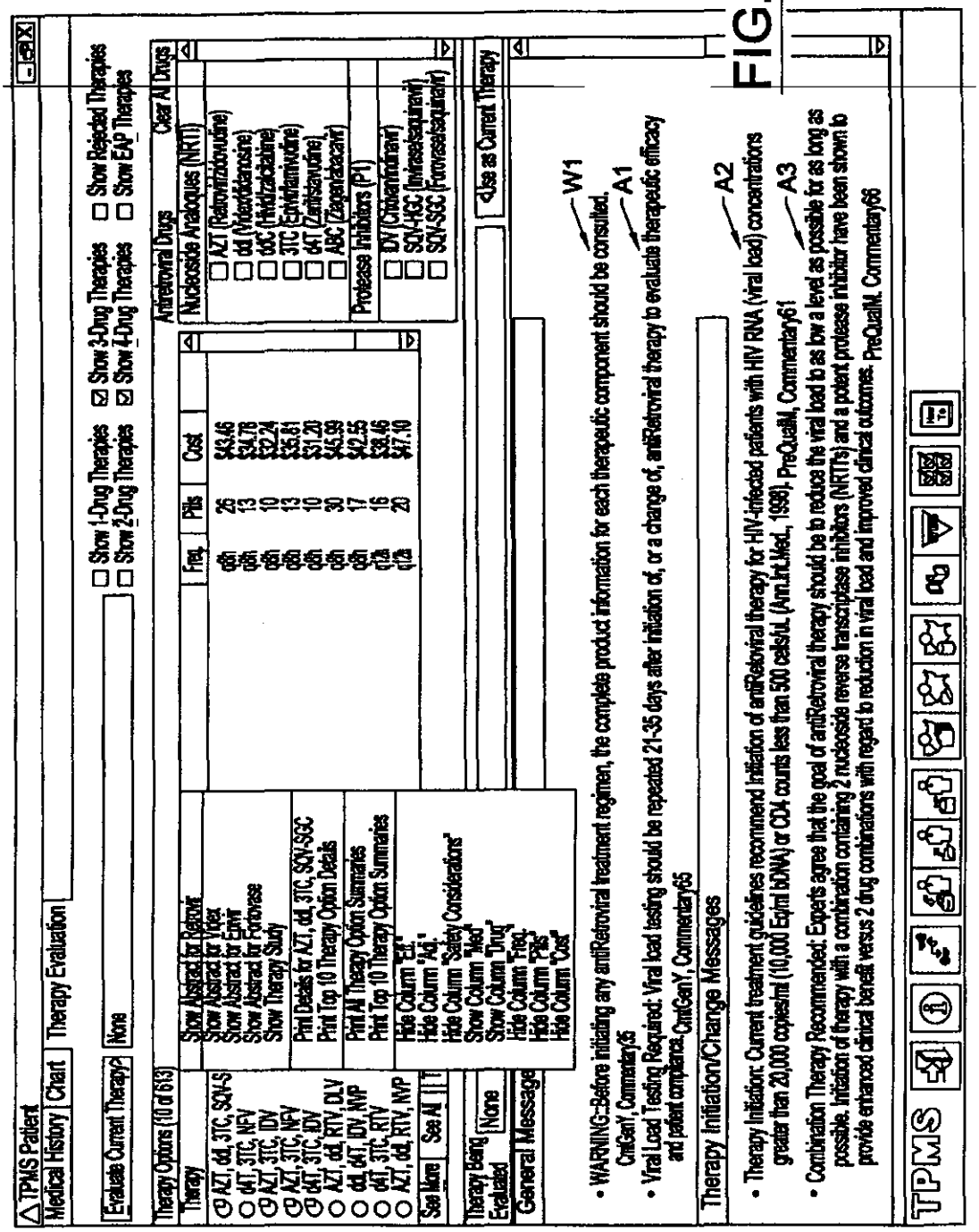


FIG. 11E.

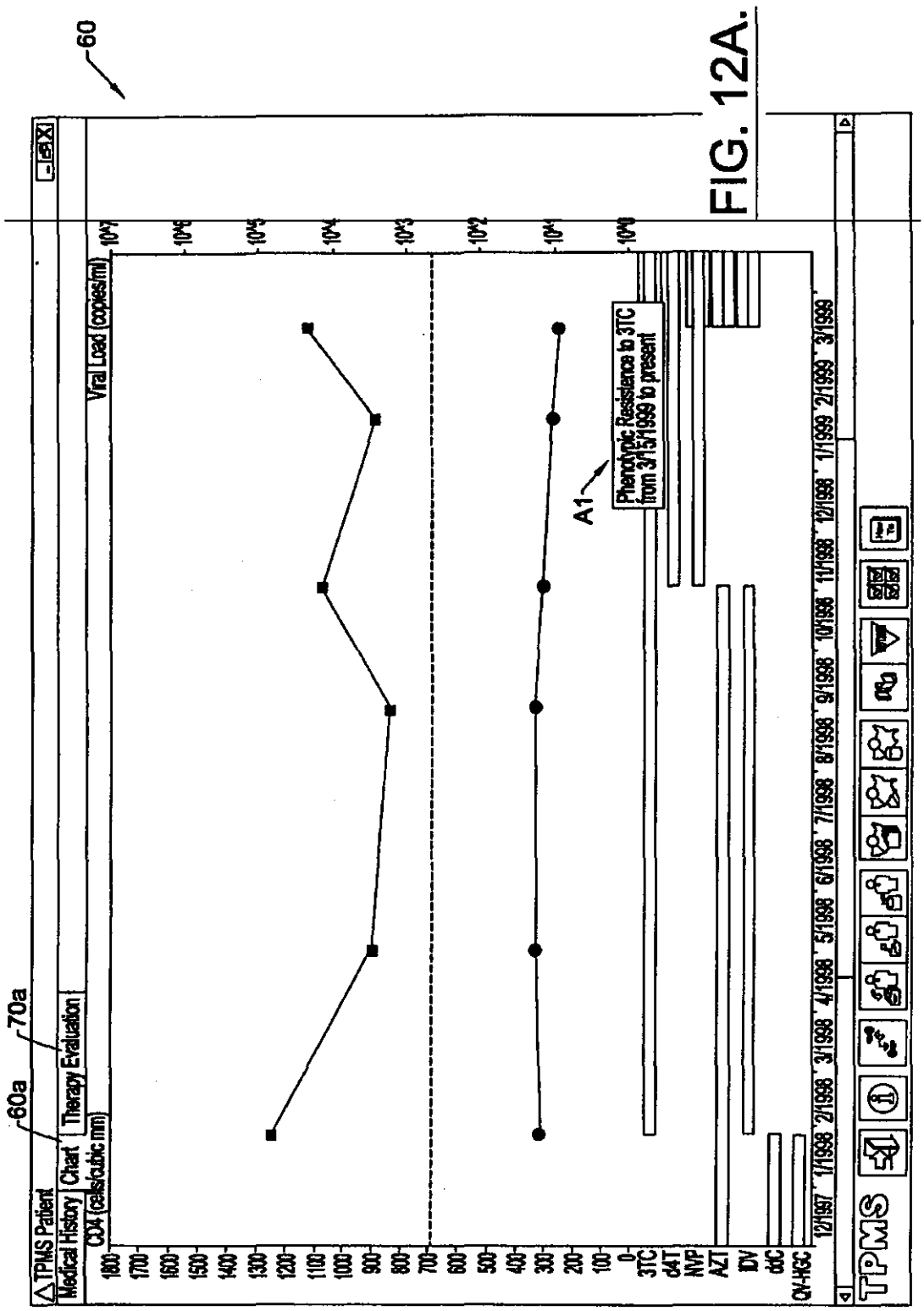


FIG. 12A.

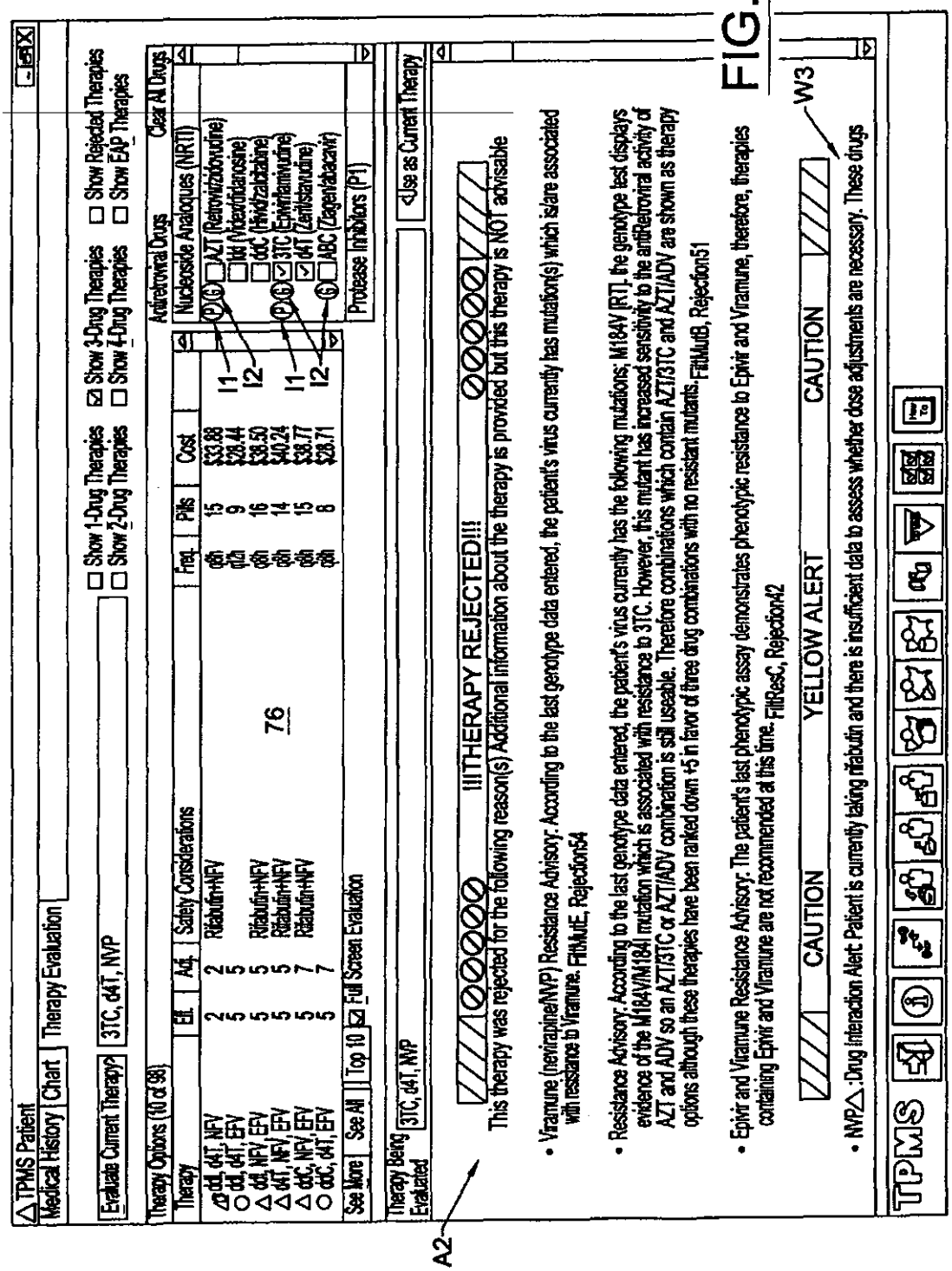


FIG. 12B.

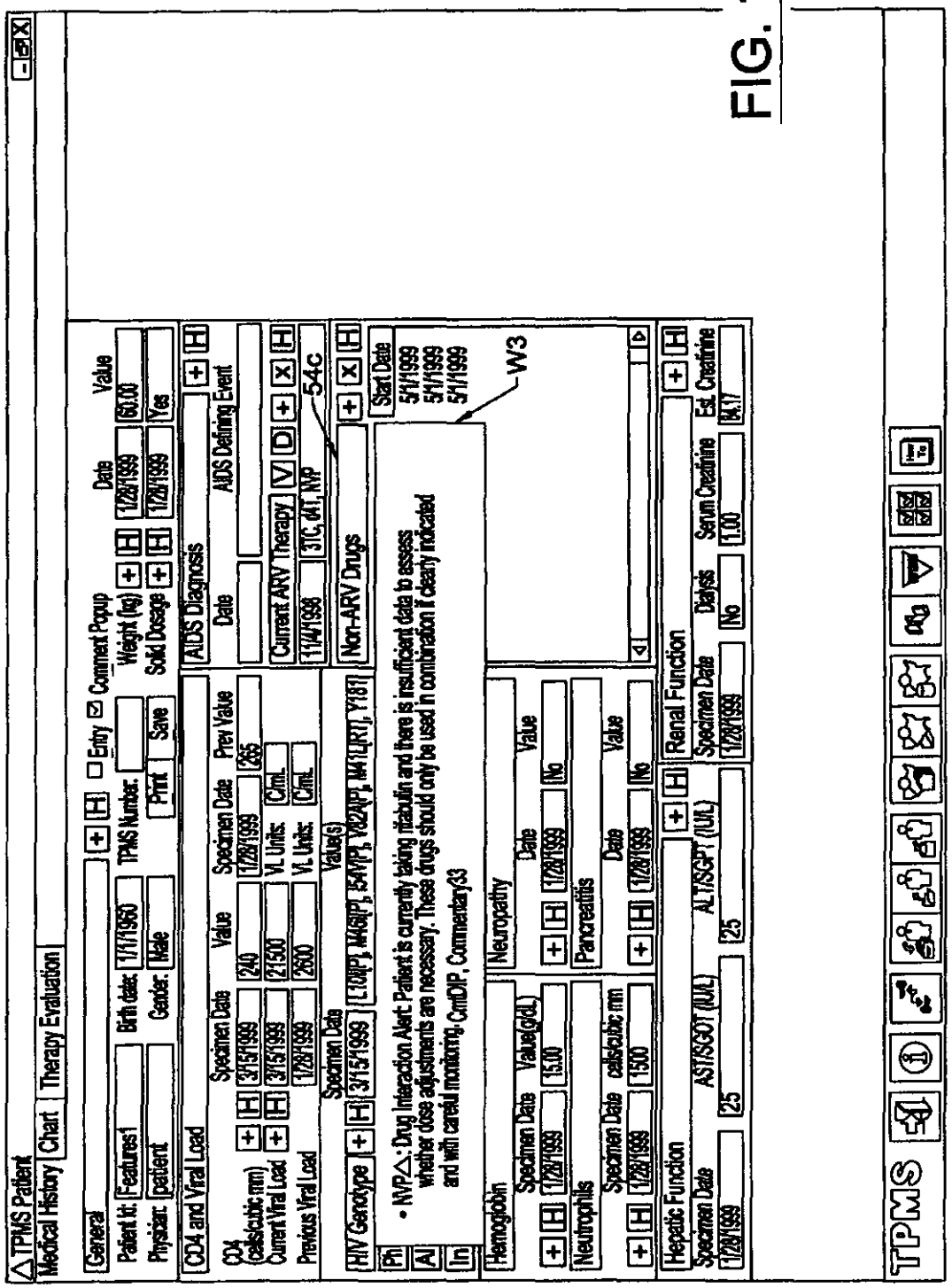


FIG. 12C.

SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/080,629 filed Apr. 3, 1998.

FIELD OF THE INVENTION

This invention concerns systems, methods and computer program products for guiding the selection of therapeutic treatment regimens for complex disorders such as cancer and HIV-1 infection, wherein a ranking of available treatment regimens is generated and advisory information clinically useful for treating patients is provided.

BACKGROUND OF THE INVENTION

Therapeutic treatment regimens for disorders such as HIV-1 infection (acquired immune deficiency syndrome or AIDS) and cancer are increasingly complex. New data and new therapeutic treatment regimens continue to modify the treatments available, and it is difficult for all but the specialist to remain current on the latest treatment information. Further, even those who are current on the latest treatment information require time to assimilate that information and understand how it relates to other treatment information in order to provide the best available treatment for a patient. Combination therapeutic treatment regimens exacerbate this problem by making potential drug interactions even more complex. Finally, an increasingly sophisticated patient population, in the face of a vast volume of consumer information on the treatment of disease, makes the mere statement of a treatment regime, without explanation, difficult for the patient to accept.

R. Miller et al., *Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems*, Ann. Intern. Med. 127, 842–845 (1997), describes policy guidelines indicating the desirability of systems that generate advice for clinician users in a manner that users can easily override. Solutions to this need are neither suggested nor disclosed.

M. Pazzani et al., *Application of an Expert System in the Management of HIV-Infected Patients*, J. Acquired Immune Deficiency Syndromes and Human Retrovirology 15, 356–362 (1997) (accepted May 12, 1997), describes a rule-based expert system by which protease, reverse transcriptase, and integrase segments of HIV are cloned and entered into an expert system that recommends two, three, and four drug regimens. A means for easily overriding the advice given is neither suggested nor disclosed.

U.S. Pat. No. 5,672,154 to Sillen describes a method for giving patients individualized, situation-dependent medication advice. The recommended type of medicine may include at least two different medicines. No means for ranking multiple treatment options is disclosed, and no means for explaining why treatment options were rejected is given. Rather, this system is primarily concerned with generating new rules from patient information to optimize a particular therapy for diseases such as Parkinson's disease, epilepsy and abnormal blood pressure.

U.S. Pat. No. 5,694,950 to McMichael describes a method and system for use in treating a patient with immunosuppressants such as cyclosporin. An expert system is employed to generate a recommendation on whether the immunosuppressant dosage should be changed and, if so, how. Ranking or selection among a plurality of different combination therapeutic treatment regimens is not suggested.

U.S. Pat. No. 5,594,638 to Iliff describes a medical diagnostic system that provides medical advice to the general public over a telephone network. This system is not concerned with generating a recommendation for a combination therapeutic treatment regimen for a known disease (see also U.S. Pat. No. 5,660,176 to Iliff).

SUMMARY OF THE INVENTION

In view of the foregoing, an object of the invention is to provide systems, methods and computer program products for selecting therapeutic treatment regimens for patients in which available treatments are listed, and optionally ranked, while unavailable or rejected treatment regimens (e.g., regimens that would not be effective, or would be dangerous) are not displayed or are assigned a low rank and are indicated to a user as not likely to be efficacious, or not preferred due to patient-specific complicating factors such as drug interaction from concomitant medications.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the available treatment options can be readily understood.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the implications of selecting a particular treatment regimen can be readily understood.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the reasons for rejection of a particular regimen can be readily understood.

A still further object of the invention is to provide systems, methods and computer program products for obtaining information about the efficacy of previous treatment regimens imposed on patients.

A method of the present invention includes providing patient information to a computing device that includes various knowledge bases. For example, a first knowledge base may include a plurality of different therapeutic treatment regimens for a disease or medical condition. A second knowledge base may include a plurality of expert rules for selecting a therapeutic treatment regimen for the disease or medical condition. A third knowledge base may include advisory information useful for the treatment of a patient with different constituents of different therapeutic treatment regimens. A fourth knowledge base may include information about past therapies, such as how a patient has fared under previous therapies.

A listing (preferably a ranked listing) of therapeutic treatment regimens for a patient is generated in the computing device. Advisory information for one or more treatment regimens in the listing is generated in the computing device based on the patient information and the expert rules.

In a preferred embodiment, the method described above further includes entering a user-defined therapeutic treatment regimen for the disease (or medical condition) that

may not be displayed from the system knowledge base-generated therapeutic treatment regimens, and generating in the computing device advisory information for the user-defined combination therapeutic treatment regimen.

In addition, in a preferred embodiment, the method described above further includes entering a rejected therapeutic treatment regimen for the disease (or medical condition) that is included in the first knowledge base but not recommended from the ranking (or given a very low ranking), and generating in the computing device advisory information for the non-recommended/low ranked therapeutic treatment regimen, wherein the advisory information includes at least one reason for not recommending (or low ranking) the therapeutic treatment regimen.

Further objects and aspects of the present invention are explained in detail in the drawings herein and the specification set forth below.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate embodiments of the invention and, together with the description, serve to explain principles of the invention.

FIG. **1** illustrates a process of the instant invention, including routines for entering a user-defined therapeutic treatment regimen and for entering a "non-recommended" therapeutic treatment regimen.

FIG. **2** schematically illustrates a system or apparatus of the present invention.

FIG. **3** illustrates a client-server environment within which the system of FIG. **2** may operate, according to an embodiment of the present invention, and wherein a central server is accessible by at least one local server via a computer network, such as the Internet, and wherein each local server is accessible by at least one client.

FIG. **4** illustrates a medical history user interface for entering data about a patient's medical history according to the present invention.

FIG. **5** illustrate a user interface chart for monitoring a patient's condition during a particular therapeutic treatment regimen over a period of time according to the present invention.

FIG. **6** illustrates a therapy evaluation user interface that facilitates evaluation of various therapeutic treatment regimen options with respect to relative efficacy, individualized adjusted relative efficacy, dosage, frequency, cost, medical complications and drug interactions according to the present invention.

FIG. **7** illustrates various symbols for providing information about a therapeutic treatment regimen option within the therapy list box of the therapy evaluation user interface of FIG. **6** according to the present invention.

FIG. **8** illustrates the therapy details box of FIG. **6** in "full screen" mode.

FIG. **9** illustrates a pop-up menu including an indexed electronic link to a PDR® that can be activated from within the therapy list box of the therapy evaluation user interface of FIG. **6** according to the present invention.

FIGS. **10A–10D** illustrate various functions of the present invention as described in Example 1.

FIGS. **11A–11E** illustrate various functions of the present invention as described in Example 2.

FIGS. **12A–12C** illustrate various functions of the present invention as described in Example 3.

DETAILED DESCRIPTION OF THE INVENTION

The present invention now will be described more fully hereinafter with reference to the accompanying drawings, in which preferred embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art. Like numbers refer to like elements throughout.

As will be appreciated by one of skill in the art, the present invention may be embodied as a method, data processing system, or computer program product. Accordingly, the present invention may take the form of an entirely hardware embodiment, an entirely software embodiment, or an embodiment combining software and hardware aspects. Furthermore, the present invention may take the form of a computer program product on a computer-usable storage medium having computer readable program code means embodied in the medium. Any suitable computer readable medium may be utilized including, but not limited to, hard disks, CD-ROMs, optical storage devices, and magnetic storage devices.

The present invention is described below with reference to flowchart illustrations of methods, apparatus (systems), and computer program products according to an embodiment of the invention. It will be understood that each block of the flowchart illustrations, and combinations of blocks in the flowchart illustrations, can be implemented by computer program instructions. These computer program instructions may be provided to a processor of a general purpose computer, special purpose computer, or other programmable data processing apparatus to produce a machine, such that the instructions, which execute via the processor of the computer or other programmable data processing apparatus, create means for implementing the functions specified in the flowchart block or blocks.

These computer program instructions may also be stored in a computer-readable memory that can direct a computer or other programmable data processing apparatus to function in a particular manner, such that the instructions stored in the computer-readable memory produce an article of manufacture including instruction means which implement the function specified in the flowchart block or blocks.

The computer program instructions may also be loaded onto a computer or other programmable data processing apparatus to cause a series of operational steps to be performed on the computer or other programmable apparatus to produce a computer implemented process such that the instructions which execute on the computer or other programmable apparatus provide steps for implementing the functions specified in the flowchart block or blocks.

A method of the instant invention is illustrated in FIG. **1**. In the first step **10**, the patient is examined to determine patient information. Examples of patient information that may be gathered include one or more of gender, age, weight, $CD4^+$ cell information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, and information for drug treatments for other conditions. The information may include historical information on prior therapeutic treatment regimens for the disease or medical condition. While the patient

is typically examined on a first visit to determine the patient information, it will be appreciated that patient information may also be stored in the computing device, or transferred to the computing device from another computing device, storage device, or hard copy, when the information has been previously determined.

The patient information is then provided 11 to a computing device that contains a knowledge base of treatments, contains a knowledge base of expert rules for determining available treatment options for the patient in light of the patient information, and also contains a knowledge base of advisory information. A list of available treatments for the patient is then generated 12 from the patient information and the available treatments by the expert rules, and advisory information for the available treatments is generated 13. The advisory information may include warnings to take the patient off a contraindicated drug or select a suitable non contraindicated drug to treat the condition before initiating a corresponding treatment regimen and/or information clinically useful to implement a corresponding therapeutic treatment regimen.

For example, when the known disease is HIV-1 infection, the treatment regimen includes antiretroviral drugs, and the treatment regimen or advisory information may also include contraindicated or potentially adversely interacting non-antiretroviral drugs. Particularly, when the treatment regimen includes a protease inhibitor. A contraindicated drug may be terfenadine. When the treatment regimen includes indinavir, a contraindicated drug is cisapride.

Exemplary antiretroviral drugs are listed below in Table 1.

TABLE 1

Abbreviation	Formal Name	Generic Name
ABC	ZIAGEN ®	Abacavir
ADV	PREVEON ®	Adefovir
APV	AGENERASE ®	Amprenavir
AZT	RETROVIR ®	Zidovudine
ddI	VIDEX ®	Didanosine
ddC	HIVID ®	Zalcitabine
d4T	ZERIT ®	Stavudine
EFV	SUSTIVA ®	Efavirenz
3TC	EPIVIR ®	Lamivudine
SQV	INVIRASE ® FORTOVASE ®	Saquinavir
IDV	CRIXIVAN ®	Indinavir
RTV	NORVIR ®	Ritonavir
DLV	RESCRIPTOR ®	Delavirdine
NFV	VIRACEPT ®	Nelfinavir
NVP	VIRAMUNE ®	Nevirapine

Exemplary advisory information that can be displayed to a user is summarized below in Table 2.

TABLE 2

	Description
Drug Therapies (All the output data types below are associated with a therapy)	The inference engine will process every therapy from a resource file which contains all valid therapy combinations. The system will support multiple drug combinations. Those therapies which are recommended by the knowledge base will be displayed along with all the data types below.
Commentaries	Commentaries consist of warnings and advisories concerning drugs as well as various patient conditions. Each commentary will appear in specific locations of the User Interface. Commentaries will have various Flags, Triggers, and Output Locations.

TABLE 2-continued

	Description
Rejection Notices	Rejection Notices are the explanation why a given therapy is not recommended. Rejection notices always appear in predefined places in the User Interface.
Cost	The cost per day is calculated for each therapy by the inference engine as well as each drug cost within a therapy.
Dosage	The base dosage and any adjustments to the base dosage due to various patient conditions are calculated by the inference engine.
Pill Burden	The number of pills in the therapy.
Frequency	Number of times the patient will be taking medications for a given therapy. For a multi-drug therapy, the Frequency of the therapy is the drug in the therapy that has the highest number of Frequencies. If a three-drug regimen has 2 drugs with q12h dosages and one that is a q8h, the therapy is considered to be a q8h Frequency.
Admin	Special drug administration instructions.
Efficacy	The relative Efficacy is a whole number that represents the relative efficacy of the various therapies. One is the most effective therapy.
Adjusted Score	The "Adjusted Score" is the Efficacy adjusted up or down based on patient specific characteristics to roughly indicate the likelihood of that therapy being an effective treatment for that patient. An example would be: the system evaluates a therapy containing a drug that is known to be associated with a medical condition in that patient's medical history, therefore the therapy is ranked low. The Ranking Ordinal is an integer, beginning with 0 and having no upper limit. A therapy with a 1 Ranking Ordinal (RO = 1) would be ranked at the top of the list whereas a therapy with a 10 Ranking Ordinal (RO = 10) would be less likely to be successful given the patient's specific history and characteristics. Each therapy will have a starting RO number which will be the therapy's relative efficacy score. The relative efficacy score can then be adjusted up or down by the rules. Both base "Efficacy" number and the "Adjusted Score" number can be displayed.

Diseases (or medical conditions), the treatment of which may be facilitated or improved by the present invention, are those for which multiple different therapy options are available for selection and treatment. Such diseases and medical conditions include, but are not limited to, cardiovascular disease (including but not limited to congestive heart failure, hypertension, hyperlipidemia and angina), pulmonary disease (including but not limited to chronic obstructive pulmonary disease, asthma, pneumonia, cystic fibrosis, and tuberculosis), neurologic disease (including but not limited to Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, amyotrophic lateral sclerosis or ALS, psychoses such as schizophrenia and organic brain syndrome, neuroses, including anxiety, depression and bipolar disorder), hepatitis infections (including hepatitis B and hepatitis C infection), urinary tract infections, venereal disease, cancer (including but not limited to breast, lung, prostate, and colon cancer), etc. It should be appreciated that prevention of development or onset of the above-mentioned diseases and medical conditions may be facilitated or improved by the present invention.

The present invention is useful for known diseases such as HIV-1 infection (acquired immune deficiency syndrome or "AIDS"), or where the known disease is any medical condition for which a combination therapeutic treatment regimen can be used. The invention is particularly useful when the list of available treatments includes a plurality (e.g., 2, 10 or 15 or more) of treatment, combination therapeutic treatment regimens (e.g., therapeutic treatment regimens incorporating two or more active therapeutic agents), where the potential for drug interactions is increased and/or the complexity involved in selecting the best available treatment is multifactorial.

Advantageously, the list of available treatments and advisory information may be regenerated in a number of ways. The patient information may be simply modified 18. In addition, if a particular therapy in which the user might be interested is not presented, a user-defined therapy may be entered 14 and advisory information generated 15 based on the user-defined therapy. Still further, if a therapeutic treatment regimen that is in the knowledge base is rejected by the system (not recommended upon display), the non-recommended therapeutic treatment regimen may be entered 16 and advisory information generated 17 for the non-recommended therapeutic treatment regimen. This may indicate to the user that they should discontinue use of a non-critical drug for another condition or select a suitable substitute that does not create a conflict/non-recommended situation so that they can then proceed with the therapy of choice. Alternatively, the advisory information can be generated automatically for non-recommended therapeutic treatment regimens. These various steps can be repeated in any sequence in an interactive manner to provide the user with assurance that all treatment options have been given adequate and appropriate consideration.

The terms "therapy" and "therapeutic treatment regimen" are interchangeable herein and, as used herein, mean any pharmaceutical or drug therapy, regardless of the route of delivery (e.g., oral, intraveneous, intramuscular, subcutaneous, intraarterial, intraperitoneal, intrathecal, etc.), for any disease (including both chronic and acute medical conditions, disorders, and the like). In addition, it is understood that the present invention is not limited to facilitating or improving the treatment of diseases. The present invention may be utilized to facilitate or improve the treatment of patients having various medical conditions, without limitation.

System Description

The present invention may be embodied as an expert system that provides decision support to physicians (or other health care providers) treating patients with a known disease, such as HIV infection. A system according to the present invention calculates combination antiretroviral therapy options and attaches all relevant information to those options.

As known to those of skill in the art, an expert system, also known as artificial intelligence (AI), is a computer program that can simulate the judgment and behavior of a human or an organization that has expert knowledge and experience in a particular field. An expert system typically contains a knowledge base containing accumulated experience and a set of rules for applying the knowledge base to each particular situation that is described to the program. Expert systems are well known to those of skill in the art and need not be described further herein.

The antiretroviral therapy options (combinations of antiretroviral drugs), are derived using a knowledge base consisting of a number of expert system rules and functions which in turn take into account a given patient's treatment history, current condition and laboratory values. A system according to the present invention supports the entry, storage, and analysis of patient data in a large central database. A system according to the present invention has a flexible data driven architecture and custom reporting capabilities designed to support patient therapy management and clinical drug trial activities such as screening, patient tracking and support. It is anticipated that a system according to the present invention may be used by health care providers (including physicians), clinical research scientists, and possibly healthcare organizations seeking to find the most cost-effective treatment options for patients while providing the highest standard of care.

A system 20 for carrying out the present invention is schematically illustrated in FIG. 2. The system 20 comprises a knowledge base of treatment regimens 21, which may be ranked for efficacy (e.g., by a panel of experts) or ranked according to system rules, a knowledge base of expert rules 22, a knowledge base of advisory information 23, a knowledge base of patient therapy history 24 and patient information 25. Patient information is preferably stored within a database and is configured to be updated. The knowledge bases and patient information 21–25 may be updated by an input/output system 29, which can comprise a keyboard (and/or mouse) and video monitor. Note also that, while the knowledge bases and patient data 21–25 are shown as separate blocks, the knowledge bases and patient data 21–25 can be combined together (e.g., the expert rules and the advisory information can be combined in a single database).

To carry out the method described above, the information from blocks 21–25 is provided to an inference engine 26, which generates the listing of available treatments and the corresponding advisory information from the information provided by blocks 21–25. The inference engine 26 may be implemented as hardware, software, or combinations thereof. Inference engines are known and any of a variety thereof may be used to carry out the present invention. Examples include, but are not limited to, those described in U.S. Pat. No. 5,263,127 to Barabash et al. (Method for fast rule execution of expert systems); U.S. Pat. No. 5,720,009 to Kirk et al. (Method of rule execution in an expert system using equivalence classes to group database objects); U.S. Pat. No. 5,642,471 to Paillet (Production rule filter mechanism and inference engine for expert system); U.S. Pat. No. 5,664,062 to Kim (High performance max-min circuit for a fuzzy inference engine).

High-speed inference engines are preferred so that the results of data entered are continually updated as new data is entered. As with the knowledge bases and patient information in blocks 21–25, the inference engine 26 may be a separate block from the knowledge bases and patient information blocks 21–25, or may be combined together in a common program or routine.

Note that the advisory information that is generated for any available therapy may differ from instance to instance based on differences in the patient information provided.

System Architecture

The present invention can be implemented as a system running on a stand alone computing device. Preferably, the present invention is implemented as a system in a client-server environment. As is known to those of skill in the art, a client application is the requesting program in a client-server relationship. A server application is a program that awaits and fulfills requests from client programs in the same or other computers. Client-server environments may include public networks, such as the Internet, and private networks often referred to as "intranets", local area networks (LANs) and wide area networks (WANs), virtual private networks (VPNs), frame relay or direct telephone connections. It is understood that a client application or server application, including computers hosting client and server applications, or other apparatus configured to execute program code embodied within computer usable media, operates as means for performing the various functions and carries out the methods of the various operations of the present invention.

Referring now to FIG. 3, a client-server environment 30 according to a preferred embodiment of the present invention is illustrated. The illustrated client-server environment 30 includes a central server 32 that is accessible by at least one local server 34 via a computer network 36, such as the Internet. A variety of computer network transport protocols including, but not limited to TCP/IP, can be utilized for communicating between the central server 32 and the local servers 34.

Central Server

The central server 32 includes a central database 38, such as the Microsoft® SQL Server application program, version 6.5 (available from Microsoft, Inc., Redmond, Wash.), executing thereon. The central server 32 ensures that the local servers 34 are running the most recent version of a knowledge base. The central server 32 also stores all patient data and performs various administrative functions including adding and deleting local servers and users to the system (20, FIG. 2). The central server 32 also provides authorization before a local server 34 can be utilized by a user. Patient data is preferably stored on the central server 32, thereby providing a central repository of patient data. However, it is understood that patient data can be stored on a local server 34 or on local storage media.

Local Server

Each local server 34 typically serves multiple users in a geographical location. Each local server 34 includes a server application, an inference engine, one or more knowledge bases, and a local database 39. Each local server 34 performs artificial intelligence processing for carrying out operations of the present invention. When a user logs on to a local server 34 via a client 35, the user is preferably authenticated via an identification and password, as would be understood by those skilled in the art. Once authenticated, a user is permitted access to the system (20, FIG. 2) and certain administrative privileges are assigned to the user.

Each local server 34 also communicates with the central server 32 to verify that the most up-to-date version of the knowledge base(s) and application are running on the requesting local server 34. If not, the requesting local server 34 downloads from the central server 32 the latest validated knowledge base(s) and/or application before a user session is established. Once a user has logged onto the system (20, FIG. 2) and has established a user session, all data and artificial intelligence processing is preferably performed on a local server 34. An advantage of the illustrated client-server configuration is that most of the computationally intensive work occurs on a local server 34, thereby allowing "thin" clients 35 (i.e., computing devices having minimal hardware) and optimizing system speed.

In a preferred embodiment, each local server database 39 is implemented via a Microsoft® SQL Server application program, Version 6.5. The primary purpose of each local database 39 is to store various patient identifiers and to ensure secure and authorized access to the system (20, FIG. 2) by a user. It is to be understood, however, that both central and local databases 38, 39 may be hosted on the central server 32.

Local Client

Each local client 35 also includes a client application program that consists of a graphical user interface (GUI) and a middle layer program that communicates with a local server 34. Program code for the client application program may execute entirely on a local client 35, or it may execute partly on a local client 35 and partly on a local server 34. As will be described below, a user interacts with the system (20, FIG. 2) by entering (or accessing) patient data within a GUI displayed within the client 35. The client 35 then communicates with a local server 34 for analysis of the displayed patient information.

Computer program code for carrying out operations of the present invention is preferably written in an object oriented programming language such as JAVA®, Smalltalk, or C++. However, the computer program code for carrying out operations of the present invention may also be written in conventional procedural programming languages, such as the "C" programming language, in an interpreted scripting language, such as Perl, or in a functional (or fourth generation) programming language such as Lisp, SML, or Forth.

The middle layer program of the client application includes an inference engine within a local server 34 that provides continuous on-line direction to users, and can instantly warn a user when a patient is assigned drugs or a medical condition that is contraindicated with, or antagonistic of, the patient's current antiretroviral therapy. Every time patient data is entered into the system (20, FIG. 2) or updated, or even as time passes, the inference engine evaluates the current status of the patient data, sorting, categorizing, ranking and customizing every possible antiretroviral therapy for a patient according to the specific needs of the patient.

Inference Engine

Inference engines are well known by those of skill in the art and need not be described further herein. Each knowledge base used by an inference engine according to the present invention is a collection of rules and methods authored by a clinical advisory panel of HIV-treating physicians and scientists. A knowledge base may have subjective rules, objective rules, and system-generated rules. Objective rules are based on industry established facts regarding the treatment of HIV using antiretroviral therapy and are drawn from the package insert information of antiretroviral drug manufacturers and from peer reviewed and published journal articles. An example of an objective rule would be an antiretroviral to antiretroviral contraindication such as:

Rule #1: If the eval therapy contains Zidovudine (AZT) and Stavudine (d4T), then reject the therapy.

In Rule #1, the term "eval therapy" refers to the therapy currently being analyzed by the system (20, FIG. 2). Rule #1 then states that if this therapy contains both AZT and d4T, then this therapy should not be displayed in a list of potential therapy options for the patient.

For objective rules, the present invention can be configured so as to prevent a user from receiving recommendations on new therapy options when certain crucial data on the patient has not been entered. However, it is understood that the present invention does not prevent a health care provider, such as a physician, from recording his/her therapy decisions, even if the system (20, FIG. 2) has shown reasons why that therapy may be harmful to the patient. The present invention allows a health care provider to be the final authority regarding patient therapy.

Subjective rules are based on expert opinions, observations and experience. Subjective rules are typically developed from "best practices" information based on consensus opinion of experts in the field. Such expert opinion may be

based on knowledge of the literature published or presented in the field or their own experience from clinical practice, research or clinical trials of approved and unapproved medications. A number of experts are used so that personal bias is reduced.

System generated rules are those derived from the outcomes of patients tracked in the system who received known and defined therapies and either improved, stabilized or worsened during a defined period. Because of the large number of potential combinations usable in HIV infection, this system generated database and rules derived from them are likely to encompass data beyond that achievable from objective or subjective rules databases.

The rules which comprise the various knowledge bases (**21–24**, FIG. **2**) of the present invention each have two main parts: a premise and a conclusion—also referred to as the left side and the right side, respectively. When a premise of a rule is found to be true, the action specified in the conclusion is taken. This is known to those of skill in the art as "firing" the rule. For example, consider the following rule:

Rule ID	Premise	Conclusion
FiltDComA1 - -	If the eval therapy contains ddC -	Commentary 18

The premise of the above rule is for the inference engine to determine whether or not a therapy being evaluated (i.e., "eval therapy") contains the antiretroviral drug "ddC". If a therapy does contain the antiretroviral drug ddC, the action called for by the conclusion of the rule is to attach "Commentary 18" to the therapy. Commentary 18 may be a piece of text that provides a user with the necessary information about therapies containing ddC.

Exemplary rules which may comprise one or more knowledge bases according to the present invention are listed below in Table 3.

TABLE 3

Therapy initiation/change: Rules that provide information on therapy change or initiation
Boundary condition rules: Limits for values, intervals for values to be updated
Comment Data Aging rules: These rules warn the user that the data in certain fields is getting old and that the most current values in the system will be used.
Rules that filter therapies due to drug interactions in ARV drug combinations
Rules that filter therapies due to medical conditions
Rules that filter therapies due to genotypic mutations in patient's plasma HIV
Rules that filter therapies due to phenotypic sensitivity/resistance
Antiretroviral therapy ranking rules
General dosage rules
Solid dosage rule
Dosage modifications due to ARV-ARV drug combination
Dosage modification due to ARV-NonARV interaction
Dosage modification due to medical condition
Comment determined
General commentary rules
Commentaries added due to medical conditions
Commentaries added due to drug interactions
Commentaries added due to drug combination
Delivery size rules

Using the various knowledge bases and patient information of the present invention (**21–25**, FIG. **2**), the inference engine (**26**, FIG. **2**) can evaluate potential therapy options for a patient based on a patient's medical history (including therapy history) and current laboratory values. Accordingly multiple antiretroviral drug combinations can be quickly and accurately analyzed for a particular patient. Furthermore, the inference engine can quickly provide guidance in the areas listed below in Table 4.

TABLE 4

Data Integrity	Is the patient lab and assessment data getting too old to be considered reliable? Are there conflicts between lab data such as phenotype data which indicates resistance to one or more antiretroviral drugs in the patient's current therapy and current viral load data which indicates significant viral suppression?
Therapy Performance	Should antiretroviral therapy be initiated for the patient? Is the patient's current therapy achieving good initial and long-term viral suppression or should the therapy be changed? Are there potential non-compliance issues as demonstrated by a lack of viral suppression with a regimen when current genotype or phenotype data does provide explanation for the failure by demonstrating resistance to any drugs in the patient current therapy?
Dosage	What are the base and adjusted dosages of antiretroviral drugs in a given therapy? Are there any special specific dosage administration instructions? What are options if patient can only take liquid dosage forms?
Contra-indications	Which antiretroviral drugs can be used with each other and what dosage adjustments are required? Are there any contraindications or interactions between antiretroviral drugs in patient's current therapy or potential therapies and the non-antiretroviral drugs patient is taking and if so what are they and what, if any, dosage adjustments are required?
Medical Conditions	Are there any medical conditions to be aware of in deciding an appropriate therapy for patient? What, if any, effect do current or historical medical conditions have on each therapy option?
Drug Cost and Delivery Data	How much does each therapy option cost? What is the dosing frequency of the drugs in the therapy? What is the pill count and optimum delivery size for the least number of pills?
Therapy Options	What are all the drug combination therapy options for patient? How can physician instantly assess which of the hundreds of potential combinations will be the most effective for patient? What information from the package inserts from each drug apply specifically to patient? What is the relative antiviral efficacy of each therapy? Are there special considerations that might make one therapy more or effective for patient?
Resistance	What drugs are patient's virus current genotypic or phenotypic profile known to be associated with resistance to? Which antiretroviral drugs are more effective against resistant strains when used together? Which drugs (if any) used in historical therapies are most likely to be effective if recycled into a new therapy? Can any of the drugs in patient's current therapy be recycled into the next therapy?

User Interface

Referring now to FIGS. **4–9**, exemplary user interfaces according to the present invention will be illustrated. In FIG. **4**, a medical history user interface **50** for entering data about a patient's medical history according to the present invention is illustrated. The medical history user interface **50** can be displayed by activating the "Medical History" tab **50a**. The illustrated medical history user interface **50** allows a user to create, save, update and print patient records. When a user adds a new patient, the medical history user interface **50** appears with empty data entry fields. Data entry fields for

receiving information via a GUI are well known to those of skill in the art and need not be described further herein. When a user opens a patient record for editing, the medical history user interface **50** appears with patient data in the various fields. Preferably color is used to highlight critical or required information in a patient record.

Important elements in the illustrated medical history user interface **50** include a "print" button **51** for printing a patient record and therapeutic treatment regimen details; a "save" button **52** for saving a patient record; and a "speed entry" check box **53** for allowing a user to move quickly between entry fields. In addition, there are multiple group headings **54** that divide a patient's medical history into related categories. Each group contains entry fields in which a user can add patient information. An "add" button **55** allows a user to add new information to a patient record for a selected group. A "delete" button **56** allows a user to delete patient information for a selected group (although the original information is still recorded in the database). A "history" button **57** allows a user to review a patient's historical data for each selected group.

After completing a patient's medical history, an inference engine analyzes the data and suggests whether a therapeutic treatment regimen is indicated; if an existing therapeutic treatment regimen should be continued or changed; and the best drug therapies for the selected patient. Often, more than one drug therapy is presented to the user. These drug therapies are preferably ranked according to expected efficacy, frequency in dosage, pill count, and cost. All of these factors can help the user make a decision about what therapy to use for the selected patient. When a user clicks on a drug therapy in the presented list, information is provided about the dosage regimens. Also, various warnings, such as drug interaction warnings, and notes about each drug, are presented. An appropriate drug therapy can then be selected.

In FIG. **5**, an exemplary user interface chart **60** for monitoring a patient's condition during a particular drug therapy over a period of time is illustrated. The user interface chart **60** can be displayed by activating the "Chart" tab **60*a***. The illustrated user interface chart **60** tracks the CD4 level against viral load. Along the left-hand side of the Y-axis **61** the CD4 count is plotted. Along the right-hand side of the Y-axis **61** the viral load count is plotted. The lines **62** represent the CD4 test and the viral load test as would be understood by those having skill in the art. Drug therapy for a time period is indicated within the area of the chart user interface **60** indicated as **63**. Time is plotted along the X-axis **64**, as illustrated.

In FIG. **6**, a therapy evaluation user interface **70** that facilitates evaluation of various therapy options with respect to relative efficacy, dosage, frequency, cost, medical complications and drug interactions is illustrated. The therapy evaluation user interface **70** can be displayed by activating the "Therapy Evaluation" tab **70*a***. Important elements in the illustrated therapy evaluation user interface **70** include an "Evaluate Current Therapy" button **71** for initiating an evaluation of a current therapy and a "Current Therapy" field **72** that lists a patient's current therapy. Detailed information about a patient's therapy is displayed in the therapy details box **73**. A therapy displayed within box **73** is identified in box **74**.

Multiple check boxes **75** are provided that allow a user to control how information is displayed within the therapy evaluation user interface **70**. Within the therapy list box **76**, a list of available therapies for a patient can be displayed. In the illustrated embodiment the drugs are listed in standard abbreviated form. Other information displayed with each drug may include that listed below in Table 5.

TABLE 5

Efficacy Rating	Lists the therapy according to expected effectiveness only, regardless of patient specific considerations (1 is most effective).
Adjusted Score	This number uses the Efficacy Rating as a base and then the system adjusts it up or down based on patient specific conditions (1 is most effective).
Safety Considerations	A brief two or three word summary of the alerts associated with the therapy.
Frequency	Lists the dosage frequency (q12h, q24h, etc.).
Pills	Lists the total number of pills required per day for the complete regimen.
Cost	Lists the total cost of the regimen per day.
Medical Alert	Displays a Y if there is one or more Yellow Medical Alerts and an R if there is one or more Red Medical Alerts associated with the therapy.
Drug Interaction	Displays a Y if there is one or more Yellow Drug Interaction Alerts and an R if there is one or more Red Drug Interaction Alerts associated with the therapy.

A list of available antiretroviral drugs is displayed within box **77**. A user desiring to evaluate a particular combination of drugs can click the appropriate check boxes **77*a*** to review information in the therapy details box **73**. A "Use as Current Therapy" button **78** allows a user to apply a particular therapy to a patient. Various hyperlinks **79** within the therapy details box **73** allow a user to display specific information about a therapy evaluation. For example, a user can be allowed to view a rule which is associated with the displayed text.

Resistance evaluation alerts **80** can be provided adjacent each available antiretroviral drug displayed within box **77**. For example, a blue "G" icon can be used to indicate that a patient's last genotype test contains mutations which are known to be associated with full or partial resistance to the antiretroviral drug. A red "P" icon can be used to indicate that a patient's last phenotype test demonstrates resistance to the antiretroviral drug.

Within the therapy list box **76**, various symbols (described in FIG. **7**) can be utilized to provide information about a drug therapy option. These symbols provide an instant graphical warning level for each therapy option. Some symbols, such as a red exclamation point, indicate that there is critical, possibly life threatening information in the therapy details box **73** for that therapy which must be read in order for that therapy to be properly utilized.

When a drug therapy from the therapy list box **76** is selected by a user for evaluation, the therapy details box **73** of FIG. **6** can be displayed in "full screen" mode as illustrated in FIG. **8**. Important elements in the illustrated therapy details box **73** include an identification box **73*a*** for identifying the therapy being evaluated; a "Use as Current Therapy" button **78** that allows a user to apply a particular therapy to a patient; and a "Show Therapies" button **73*b*** that returns the therapy details box **73** back to half-screen size as illustrated in FIG. **6**. In addition, various hyperlinks may be embedded within text displayed within the therapy details box **73** that can be activated by a user to display various types of information. Eye catching alert banner(s) **73*c*** and text **73*d*** can be displayed at the top of the therapy details box **73** as illustrated. Dosages **73*e*** of each drug, along with special administration instructions, can be displayed within the therapy details box **73** as illustrated. Dosage adjustment information **73*f*** and various warnings and advisories **73g** can also be displayed within the therapy details box **73** as illustrated.

According to a preferred embodiment of the present invention, therapeutic treatment regimens are not displayed to a user if an invalid drug is selected for treatment of a patient.

Physicians Desk Reference®

According to a preferred embodiment of the present invention, the Physicians Desk Reference® (PDR®) **28**, which is a known drug reference source, is fully integrated with the system **20** of FIG. **2**. Users can access the PDR® drug abstracts for antiretroviral drugs listed in the therapy list box **76** of the therapy evaluation user interface **70** of FIG. **6**. In addition, users can access the PDR® on-line Web database to obtain additional information about a specific drug or to research a substitute for a contraindicated drug. When a user selects a drug within the therapy list box **76** of the therapy evaluation user interface **70**, a web browser preferably is launched and the PDR® on-line Web database is accessed. Information can also be extracted from the PDR® on-line Web database to provide drug selection lists for non-antiretroviral drugs that a patient may be taking and to define relationships between brand name and generic drugs.

As illustrated in FIG. **9**, a PDR® pop-up menu **90** may be provided that can be activated from within the therapy list box **76** of the therapy evaluation user interface **70** of FIG. **6**. From the PDR® pop-up menu **90** a user can access various information from the PDR® including, but not limited to, drug abstracts, and generic components contained within a brand name drug.

The following non-limiting examples illustrate various aspects of the present invention. These examples are provided for illustrative purposes only, and are not intended to be limiting of the invention.

EXAMPLE 1

Example 1 will be explained with reference to FIGS. **10A–10D**. Referring to FIG. **10A**, a medical history user interface **50** containing evaluated data for patient "demo1" is illustrated. The group heading "Hemoglobin" **54*a*** has changed colors to indicate to a user that the patient has an abnormally low hemoglobin value from a previous (historical) blood sampling. When the therapy evaluation tab **70*a*** is activated to display the therapy evaluation user interface **70** (FIG. **10B**) the associated medical condition warning of a history of anemia and the caution notification if using drugs known to be associated with hematopoetic toxicity is triggered as illustrated in the therapy details box **73** of FIG. **10B**.

In addition, the group heading "Renal Function" **54*b*** in FIG. **10*a*** has changed colors to warn a user of potential renal dysfunction and is also indicated by the low estimated creatinine clearance rate in field **F1** (which the system calculates using a mathematical formula taking patient age, sex, weight, and serum creatinine values—all of which are fields of the "Medical History" user interface **50**). This information is pointed out to the user and is used if dosage adjustments are required for drugs that are known to be affected (cleared) by renal function.

Current and the next most recent CD4$^+$ cell count and viral load are displayed (F2, medical history user interface **50**). This information is also used to determine when to start or change therapy and to evaluate the initial antiviral efficacy of a newly administered antiviral regimen.

Current and historical values for all fields in the medical history user interface **50** (FIG. **10A**) can be viewed by pressing the "H" button beside fields that have this button.

In FIG. **10C**, the "Chart" user interface **60** has been activated. HIV RNA (viral load) is plotted on a log scale, the CD4 count is plotted on a linear scale, and the drug treatments are shown as Gantt bars on the horizontal date scale at the bottom of the chart user interface **60**.

In FIG. **10D**, the "Change Therapy Recommendation" message box **MB1** pops up when the "Therapy Evaluation" tab **70*a*** is selected. This box represents the processing of the data from the "Medical History" tab and the knowledge base output, including objective rules derived from published treatment guidelines, indicating that initiation of therapy, or a change of therapy in this case, may be called for if the other variable(s) indicated in the message have been addressed.

The list of available therapies and associated ranking order may be shown within the therapy details box **73** of FIG. **10B**. This represents the output of the knowledge base for therapy selection. Included with the list of therapies can be any of the following: safety advisories (dosage adjustment, drug interaction, etc.) with a yellow triangle or red exclamation warning symbols; number of pills; daily cost of all three drugs; dosing regimen (q 8h, q 12 h, etc.); and dosages for all drugs in a regimen (including dosage adjustments if necessary) and pertinent information specific to the patient is listed in the dialog box.

EXAMPLE 2

Example 2 will be explained with reference to FIGS. **11A–11E**, and relates to patient file "ARV naive1" which is an example of an HIV-infected patient who has not been treated with anti-HIV drugs previously. In FIG. **11A**, a medical history user interface **50** containing evaluated data for patient "ARV naive1" is illustrated. In FIG. **11B**, when the "Therapy Evaluation" tab **70*a*** is activated to display the therapy evaluation user interface **70**, a "Boundary and Prequalification Messages" message box **MB2** pops up indicating that according to the current, published, HIV treatment guidelines, the patient should be initiated on antiviral therapy and that the current guidelines recommend combinational therapy.

In FIG. **11C**, the therapy evaluation user interface **70** has been activated and demonstrates features/functions associated with therapy evaluation including a general warning **W1** and advisories **A1**, **A2**, and **A3** for the patient related to treatment of the disease (e.g., whether therapy should be initiated or changed) or related to a specific therapy selected from the list box which is being evaluated by the user.

FIG. **11D** illustrates various information that is displayable by clicking on an individual therapy in the therapy list box **76** of FIG. **11C**. Information displayed includes dosages of all drugs with general and patient-specific warnings and advisories.

The features available by right clicking on any therapy listed in the therapy list box **76** of FIG. **11C** are illustrated in FIG. **11E** and include: linking to an electronic PDR® to show drug package insert information or perform drug search information; showing or hiding columns of information displayed within the therapy list box; linking to a publication or abstract associated with a therapy that has a "book" icon associated therewith; and various printing functions.

EXAMPLE 3

Example 3 will be explained with reference to FIGS. **12A–12C**, and relates to patient file "Features1" which illustrates some important functions/features that a system

according to the present invention can provide for highly drug experienced patients who may have developed resistance associated with the use of several antiviral drugs. Features, including functions attributed to the new resistance and historical therapy rules are illustrated and includes:

1) Potential drug resistance advisories (**A1**, FIG. **12A**) when the chart tab **60***a* is activated, or (**A2**, FIG. **12B**) when the therapy evaluation tab **70***a* is activated;
2) The heads up "P" and "G" indicators (**I1** and **I2**, FIG. **12B**) to remind of phenotypic or genotypic resistance associated with certain anti-HIV compounds as demonstrated for this patient (including indication of expected/anticipated genotypic resistance, as a result of cross-resistance, to a drug that a patient may not be taking currently or has not previously taken);
3) The drug interaction warning system (indicated by warning **W3**, FIG. **12C**). Warning **W3** is for the interaction between Nevirapine and rifabutin (which was selected from the list of non-antiretroviral drugs available as part of the medical history user interface **50**). The drug interaction warning message may be viewed from the medical history user interface **50** by "right-clicking" the non-ARV title bar **54C**, which has turned yellow indicating the presence of an ARV-nonARV drug interaction. This information is also prominently displayed for the user on the therapy evaluation user interface **70** as a text message (**W3**, FIG. **12B**) as well as in the "Safety Considerations" section of the drug list box (**76**, FIG. **12B**); and
4) The chart user interface **60** (FIG. **12A**) illustrates the viral load, CD4, drug therapies, and associated drug resistance in graphic form for the user to evaluate.

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined in the claims. Therefore, it is to be understood that the foregoing is illustrative of the present invention and is not to be construed as limited to the specific embodiments disclosed, and that modifications to the disclosed embodiments, as well as other embodiments, are intended to be included within the scope of the appended claims. The invention is defined by the following claims, with equivalents of the claims to be included therein.

That which is claimed is:

1. A method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said method comprising:

(a) providing patient information to a computing device comprising:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) generating in said computing device a ranked listing of available therapeutic treatment regimens for said patient; and

(c) generating in said computing device advisory information for one or more therapeutic treatment regimens in said ranked listing based on said patient information and said expert rules.

2. A method according to claim **1**, further comprising the steps of:

(d) entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not included in said first knowledge base;

(e) generating in said computing device advisory information for said user-defined combination therapeutic treatment regimen.

3. A method according to claim **1**, further comprising the steps of:

(f) entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said ranked listing; and

(g) generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

4. A method according to claim **1**, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

5. A method according to claim **1**, said patient information including prior therapeutic treatment regimen information.

6. A method according to claim **1**, wherein said patient information includes prior patient information stored in said computing device.

7. A method according to claim **1**, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

8. A method according to claim **1**, wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

9. A method according to claim **7**, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

10. A method according to claim **7**, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

11. A method according to claim **7**, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

12. A method according to claim **1**, wherein said known disease or medical condition is one where multiple prophylactic or therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease.

13. A method according to claim **1**, wherein said known disease or medical condition is a cardiovascular disease.

14. A method according to claim **1**, wherein said known disease or medical condition is a pulmonary disease.

15. A method according to claim 1, wherein said known disease or medical condition is a neurologic disease.

16. A method according to claim 1, wherein said known disease or medical condition is cancer.

17. A method according to claim 1, wherein said known disease or medical condition is a urinary tract infection.

18. A method according to claim 1, wherein said known disease or medical condition is hepatitis.

19. A method according to claim 1, wherein said known disease or medical condition is HIV-1 infection.

20. A method according to claim 1, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

21. A method according to claim 1, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

22. A method according to claim 1, further comprising the step of:

(d) accessing, via said computing device, information for one or more therapeutic treatment regimens from a drug reference source.

23. A system for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said system comprising:

(a) a computing device comprising:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) means for providing patient information to said computing device;

(c) means for generating in said computing device a ranked listing of therapeutic treatment regimens for said patient; and

(d) means for generating in said computing device advisory information for one or more therapeutic treatment regimens in said ranked listing based on said patient information and said expert rules.

24. A system according to claim 23, further comprising:

(e) means for entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not generated or displayed via said first knowledge base;

(f) means for generating in said computing device advisory information for said user-defined combination therapeutic treatment regimen.

25. A system according to claim 23, further comprising:

(f) means for entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said ranked listing; and

(g) means for generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

26. A system according to claim 23, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

27. A system according to claim 23, said patient information including prior therapeutic treatment regimen information.

28. A system according to claim 23, wherein said patient information includes prior patient information stored in said computing device.

29. A system according to claim 23, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

30. A system according to claim 23, wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

31. A system according to claim 29, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

32. A system according to claim 29, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

33. A system according to claim 29, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

34. A system according to claim 23, wherein said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease or medical condition.

35. A system according to claim 23, wherein said known disease or medical condition is a cardiovascular disease.

36. A system according to claim 23, wherein said known disease or medical condition is a pulmonary disease.

37. A system according to claim 23, wherein said known disease or medical condition is a neurologic disease.

38. A system according to claim 23, wherein said known disease or medical condition is cancer.

39. A system according to claim 23, wherein said known disease or medical condition is a urinary tract infection.

40. A system according to claim 23, wherein said known disease or medical condition is hepatitis.

41. A system according to claim 23, wherein said known disease or medical condition is HIV-1 infection.

42. A system according to claim 23, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

43. A system according to claim 23, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

44. A system according to claim 23, further comprising:

(e) means for accessing, via said computing device, information for one or more therapeutic treatment regimens from a standard drug reference source.

45. A computer program product for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said computer program product comprising a computer usable storage medium having computer readable program code means embodied in the medium, the computer readable program code means comprising:

(a) computer readable program code means for generating:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) computer readable program code means for providing patient information;

(c) computer readable program code means for generating a ranked listing of available therapeutic treatment regimens for said patient; and

(d) computer readable program code means for generating advisory information for one or more therapeutic treatment regimens in said ranked listing based on said patient information and said expert rules.

46. A computer program product according to claim **45**, further comprising:

(e) computer readable program code means for entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not generated or displayed via said first knowledge base;

(f) computer readable program code means for generating advisory information for said user-defined combination therapeutic treatment regimen.

47. A computer program product according to claim **46**, further comprising:

(g) computer readable program code means for entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said ranked listing; and

(h) computer readable program code means for generating advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

48. A computer program product according to claim **45**, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

49. A computer program product according to claim **45**, said patient information including prior therapeutic treatment regimen information.

50. A computer program product according to claim **45**, wherein said patient information includes prior patient information.

51. A computer program product according to claim **45**, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

52. A computer program product according to claim **45** wherein said computer readable program code means comprises computer readable program code means for generating a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

53. A computer program product according to claim **51**, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

54. A computer program product according to claim **51**, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

55. A computer program product according to claim **51**, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

56. A computer program product according to claim **45**, wherein said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease or medical condition.

57. A computer program product according to claim **45**, wherein said known disease or medical condition is a cardiovascular disease.

58. A computer program product according to claim **45**, wherein said known disease or medical condition is a pulmonary disease.

59. A computer program product according to claim **45**, wherein said known disease or medical condition is a neurologic disease.

60. A computer program product according to claim **45**, wherein said known disease or medical condition is cancer.

61. A computer program product according to claim **45**, wherein said known disease or medical condition is a urinary tract infection.

62. A computer program product according to claim **45**, wherein said known disease or medical condition is hepatitis.

63. A computer program product according to claim **45**, wherein said known disease or medical condition is HIV-1 infection.

64. A computer program product according to claim **45**, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

65. A computer program product according to claim **45**, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

66. A computer program product according to claim **45**, further comprising:

(e) computer readable program code means for accessing information for one or more therapeutic treatment regimens from a standard drug reference source.

* * * * *

US006188988B1

(12) **United States Patent**
Barry et al.

(10) **Patent No.: US 6,188,988 B1**
(45) **Date of Patent: *Feb. 13, 2001**

(54) **SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS**

(75) Inventors: **David W. Barry**, Chapel Hill; **Carolyn S. Underwood**, Cary; **Bruce J. McCreedy**, Raleigh; **David D. Hadden**, Durham, all of NC (US); **Jason L. Lucas**, West Chester, PA (US)

(73) Assignee: **Triangle Pharmaceuticals, Inc.**, Durham, NC (US)

(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/523,532**

(22) Filed: **Mar. 10, 2000**

Related U.S. Application Data

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(60) Provisional application No. 60/080,629, filed on Apr. 3, 1998.

(51) **Int. Cl.**[7] **G06F 17/60**
(52) **U.S. Cl.** 705/3; 705/2; 706/45; 706/46; 706/47; 706/924
(58) **Field of Search** 705/2, 3, 1; 706/45, 706/46, 47, 10, 61, 924

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,839,822 * 6/1989 Dormond et al. 706/45
4,868,763 * 9/1989 Masui et al. 706/10

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

WO 97/29447 * 8/1997 (WO).

OTHER PUBLICATIONS

Miller et al.; *Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems, Annals of Internal Medicine,* 127(9):842–845 (1997).

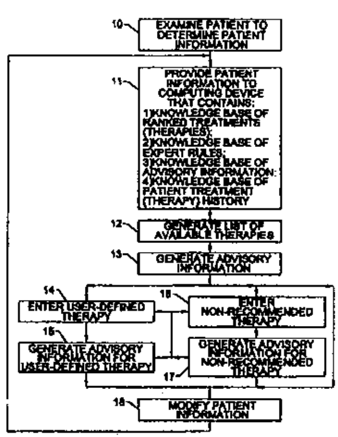
(List continued on next page.)

Primary Examiner—Emanuel Todd Voeltz
Assistant Examiner—John W. Hayes
(74) *Attorney, Agent, or Firm*—Myers Bigel Sibley & Sajovec

(57) **ABSTRACT**

Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen for a known disease such as HIV infection are disclosed. The method comprises (a) providing patient information to a computing device (the computer device comprising: a first knowledge base comprising a plurality of different therapeutic treatment regimens for the disease; a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for the disease; and a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of the different therapeutic treatment regimens; and (b) generating in the computing device a listing (preferably a ranked listing) of therapeutic treatment regimens for the patient; and (c) generating in the computing device advisory information for one or more treatment regimens in the listing based on the patient information and the expert rules.

66 Claims, 22 Drawing Sheets



U.S. PATENT DOCUMENTS

5,299,121	*	3/1994	Brill et al.	705/2
5,342,922	*	8/1994	Marshall et al.	530/329
5,355,444	*	10/1994	Chirico	706/45
5,517,405	*	5/1996	McAndrew	705/2
5,594,638	*	1/1997	Iliff	705/3
5,660,176	*	8/1997	Iliff	600/300
5,672,154	*	9/1997	Sillen et al.	604/503
5,694,950	*	12/1997	McMichael	128/898
5,737,539	*	4/1998	Edelson et al.	705/3
5,845,255	*	12/1998	Mayaud	705/3
5,908,383	*	6/1999	Brynjestad	600/300
5,911,132	*	6/1999	Sloane	705/3
5,924,074	*	7/1999	Evans	705/3
5,950,630	*	9/1999	Portwood et al.	705/3
6,014,631	*	1/2000	Teagarden et al.	705/3
6,021,404	*	2/2000	Moukheibir	706/46
6,049,794	*	4/2000	Jacobs et al.	706/45
6,081,786	*	6/2000	Barry et al.	705/3
6,108,635	*	8/2000	Herren et al.	705/2

OTHER PUBLICATIONS

Ziporyn, Terra, "Computer–Assisted Medical Decision–aking: Interest Growing", The Journal of the American Medical Association, pp. 913–918, Aug. 27, 1982.*

Barnett, G. et al. "DXplain; An Evolving Diagnostic Decision–Support System", The Journal of the American Medical Association, pp. 67–74, Jul. 3, 1987.*

Merz, Beverly, "Artificial Intelligence Charts role in Medicine", american Medical News, vol. 33, No. 2, p. 3, Jan. 12, 1990.*

Wyatt, Jeremy, "Computer–Based Knowledge Systems", Lancet, vol. 338, No. 8780, pp. 1431–1437, Dec. 7, 1991.*

Silverman, Barry G., "Survey of Expert Critiquing Systems: Practical and Theoretical Frontiers", Communications of the ACM, vol. 35, No. 4, pp. 106–127, Apr. 1992.*

Molino et al, "CARE: A Knowledge–Based System for Assisting the Physician in Patient Management", Artificial Intelligence in Medecine, Strategies for Medical Reasoning–Patient Management, 1993.*

Johnson, Kevin B., "American Journal of Diseases in Children", Dialog File 442:AMA Journals, Dec. 1995.*

Ruffin, Marshall, "Information Technology, Part 2: Interactive Media Enhances Medicine", Physician Executive, vol. 22, Issue 8, Aug. 1996.*

McCormack, John, "Research Takes on a Second Life", Health Data Management, p. 25, Nov. 1996.*

Pazanni et al, "Application of an Expert System in the Management of HIV–Infected Patients", Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, vol. 15, No. 5, pp. 356–362.*

"UCSF Launches Website HIV Insite, A Comprehensive Online Gateway to AIDS Knowledge", Business Wire, Dialog File 148: Trade & Industry Database, Mar. 17, 1997.*

Detmer, William et al, "Using the Internet to Improve Knowledge Diffusion in Medicine", Communications of the ACM, vol. 40, Issue 8, pp. 101–108, Aug. 1997.*

Anderson, James G., "Clearing the Way for Physicians Use of Clinical Information Systems", Communications of the ACM, vol. 40, Issue 8, pp. 83–90, Aug. 1997.*

Walton, R. T. et al, "Evaluation of Computer Support for Prescribing (CAPSULE) Using Simulated Cases", British Medical Journal, London, vol. 315, Issue 7111, Internation Edition, pp. 791–795, Sep. 27, 1997.*

Evans et al, "A Computer–Assisted Management Program for Antibiotics and Other Antiinfective Agents", The New England Journal of Medicine, vol. 338, No. 4, pp. 232–238, Jan. 22, 1998.*

* cited by examiner

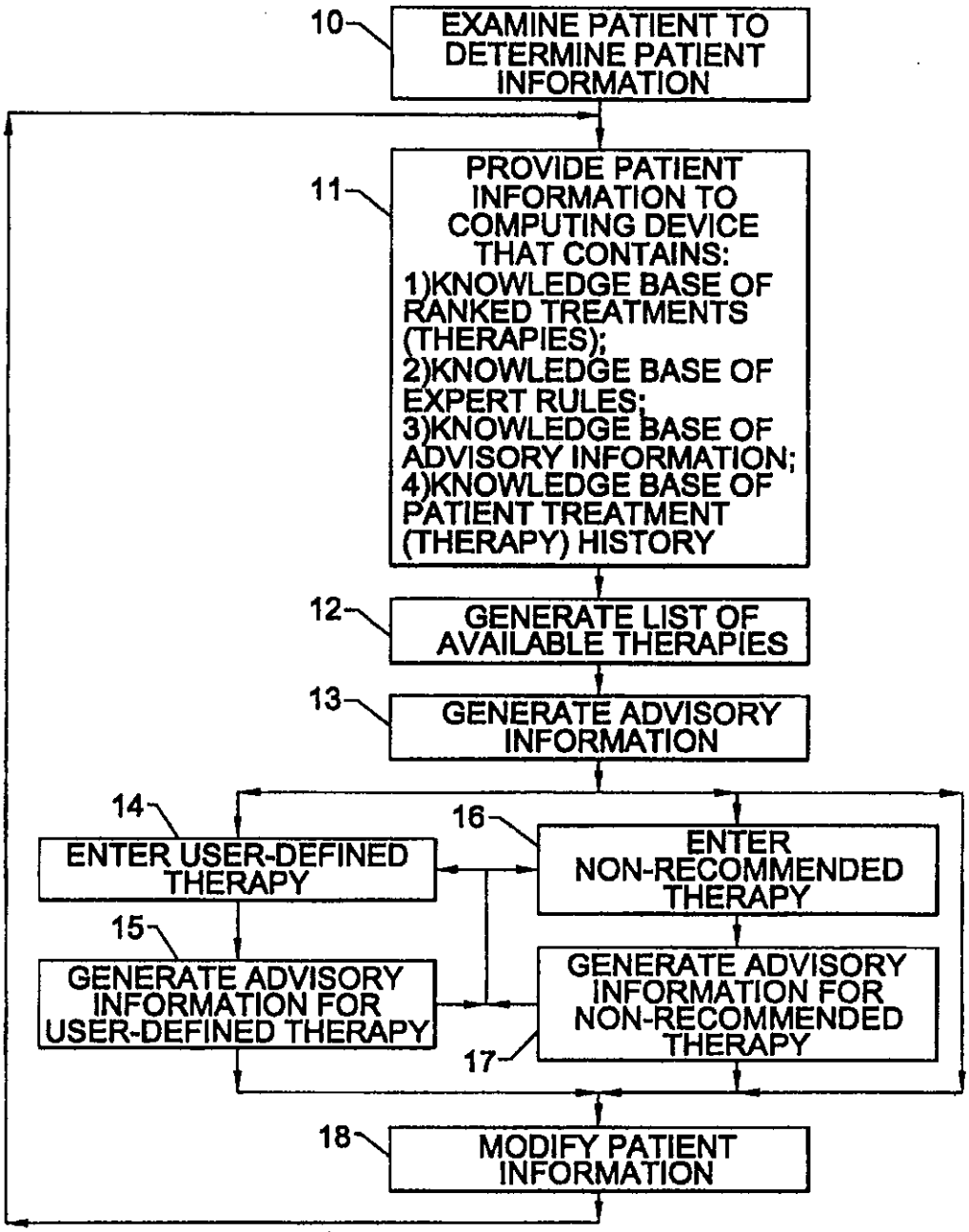

10
EXAMINE PATIENT TO DETERMINE PATIENT INFORMATION
11
PROVIDE PATIENT INFORMATION TO COMPUTING DEVICE THAT CONTAINS:
1)KNOWLEDGE BASE OF RANKED TREATMENTS (THERAPIES);
2)KNOWLEDGE BASE OF EXPERT RULES;
3)KNOWLEDGE BASE OF ADVISORY INFORMATION;
4)KNOWLEDGE BASE OF PATIENT TREATMENT (THERAPY) HISTORY
12
GENERATE LIST OF AVAILABLE THERAPIES
13
GENERATE ADVISORY INFORMATION
14
ENTER USER-DEFINED THERAPY
16
ENTER NON-RECOMMENDED THERAPY
15
GENERATE ADVISORY INFORMATION FOR USER-DEFINED THERAPY
GENERATE ADVISORY INFORMATION FOR NON-RECOMMENDED THERAPY
17
18
MODIFY PATIENT INFORMATION

FIG. 1.

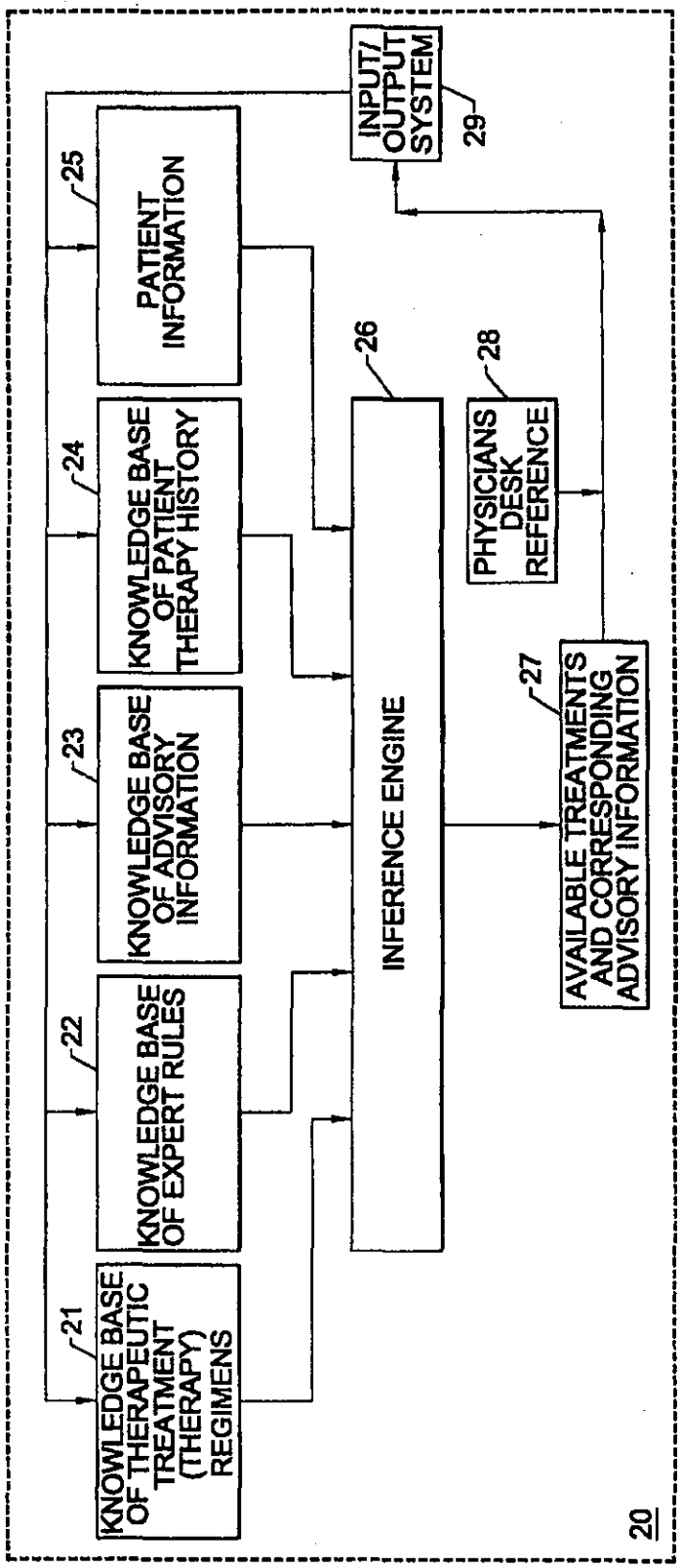


FIG. 2.

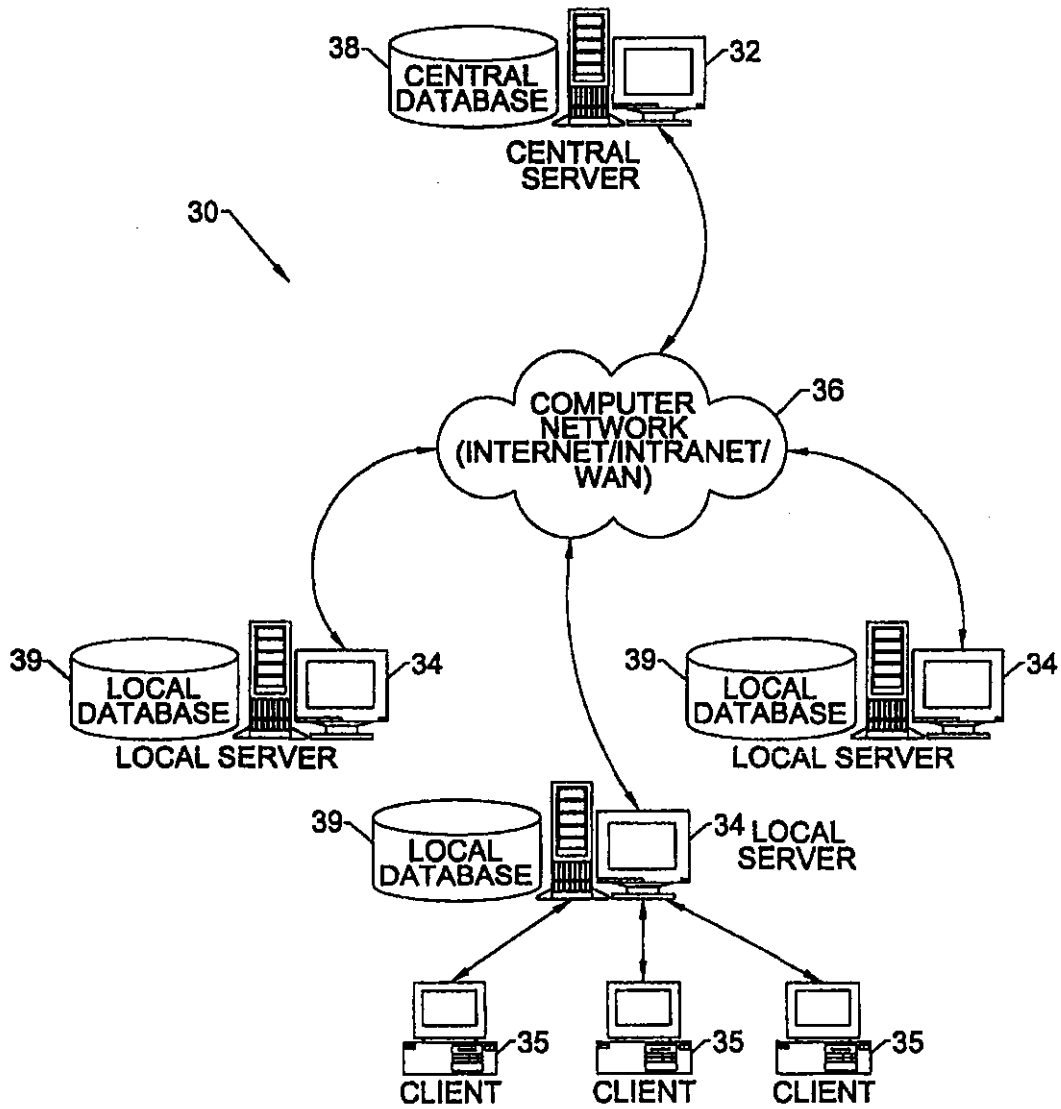

38
CENTRAL DATABASE
32
CENTRAL SERVER
30
COMPUTER NETWORK (INTERNET/INTRANET/ WAN)
36
39
LOCAL DATABASE
34
LOCAL SERVER
39
LOCAL DATABASE
34
LOCAL SERVER
39
LOCAL DATABASE
34 LOCAL SERVER
35
CLIENT
35
CLIENT
35
CLIENT

FIG. 3.

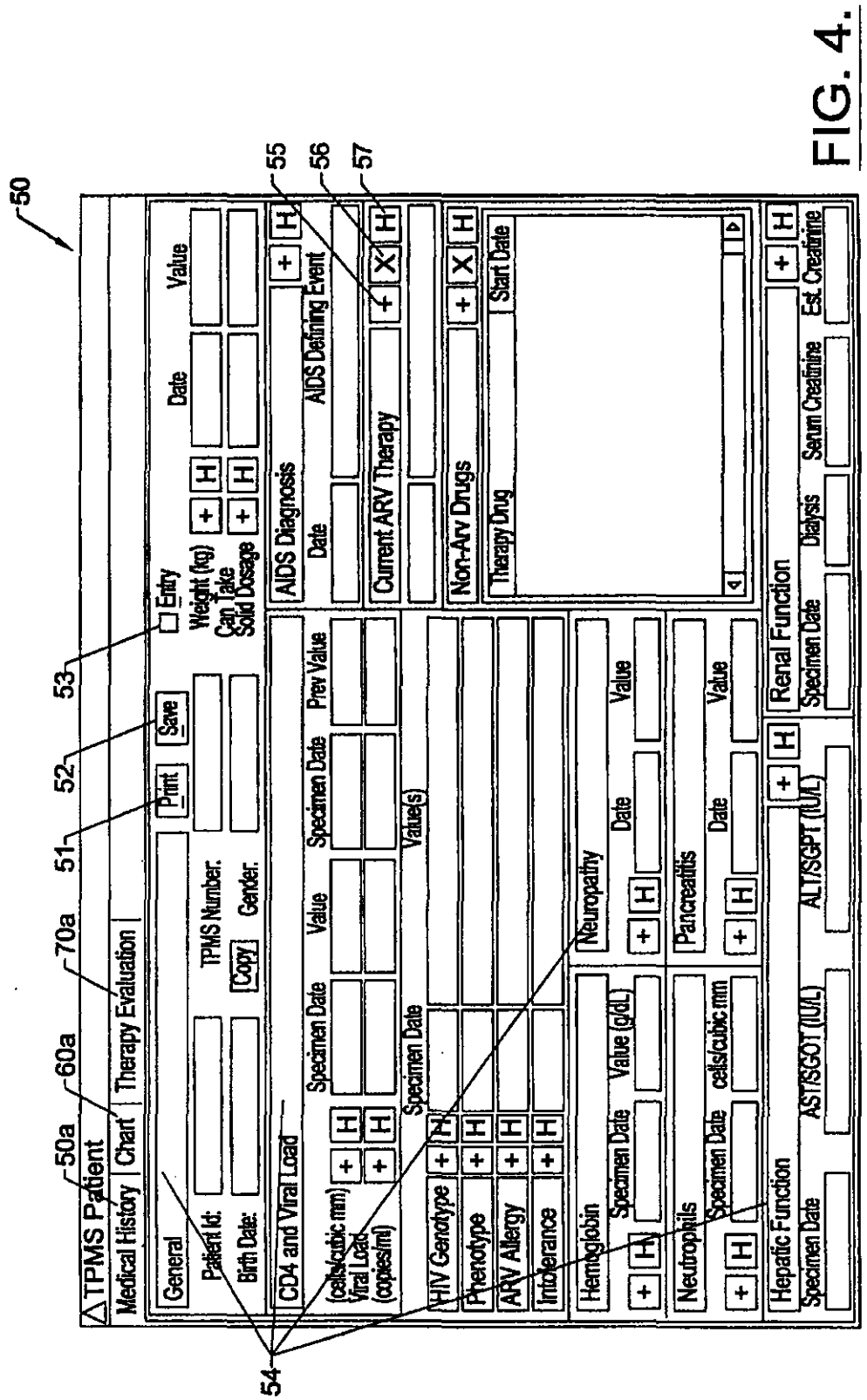


FIG. 4.

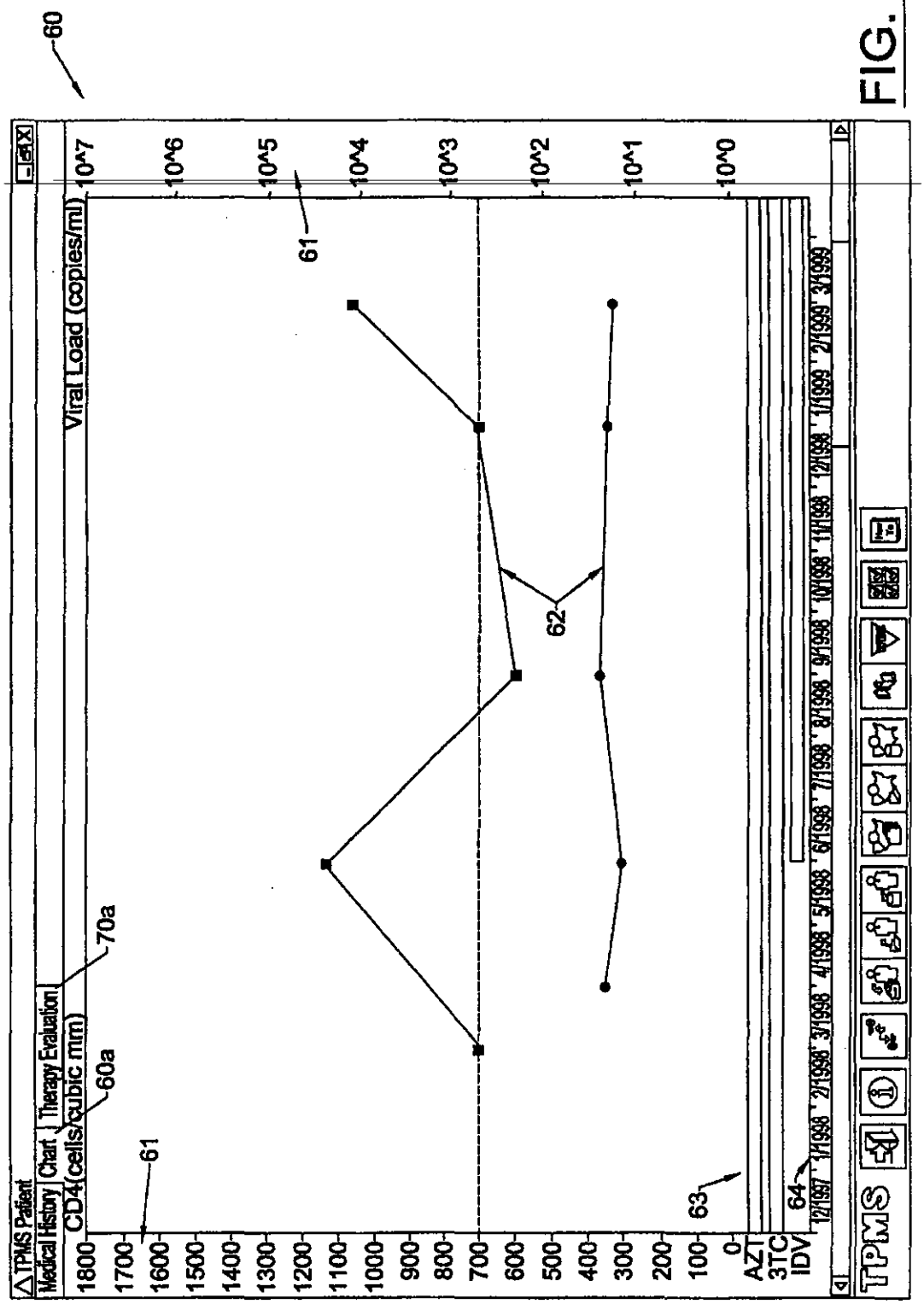
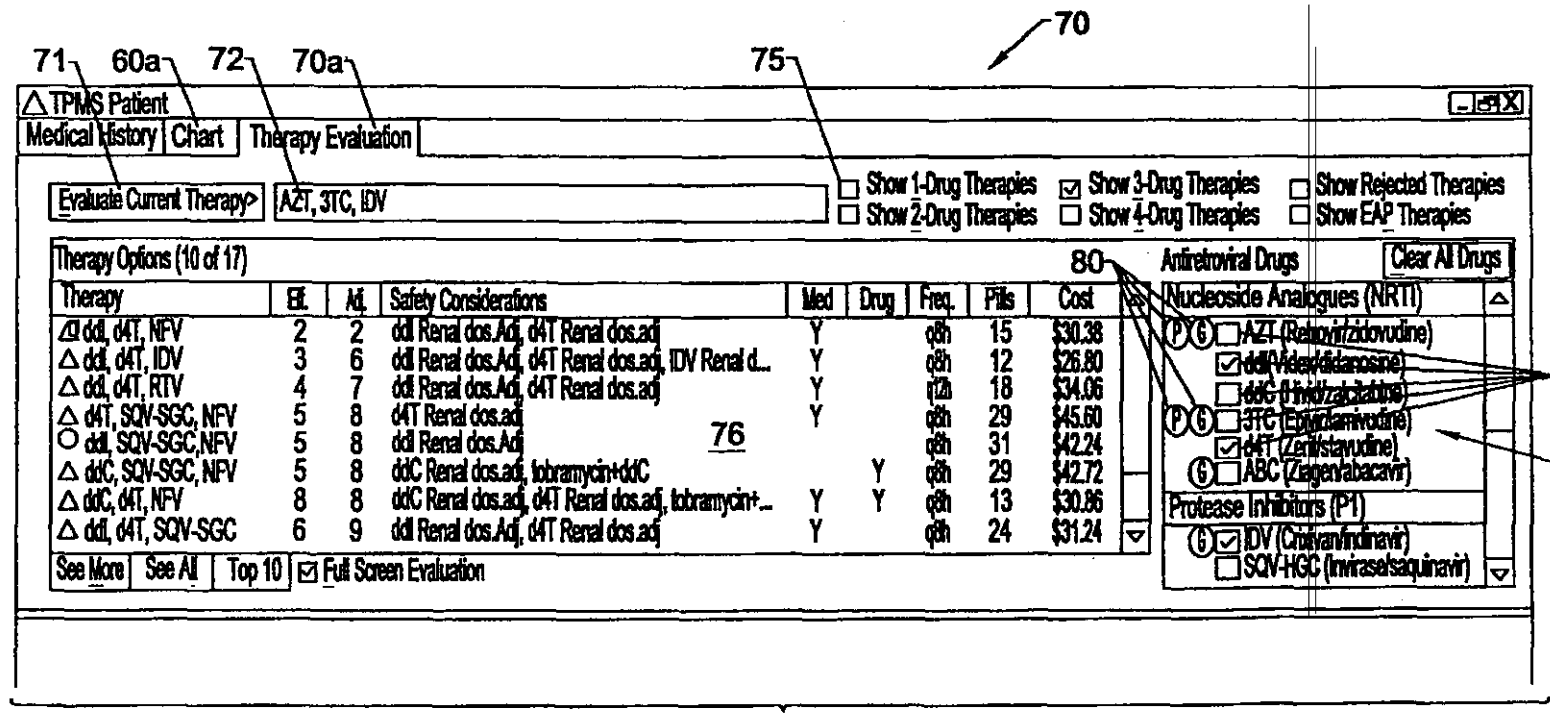


FIG. 5.



TO FIG. 6B.

FIG. 6A.

FROM FIG. 6A.

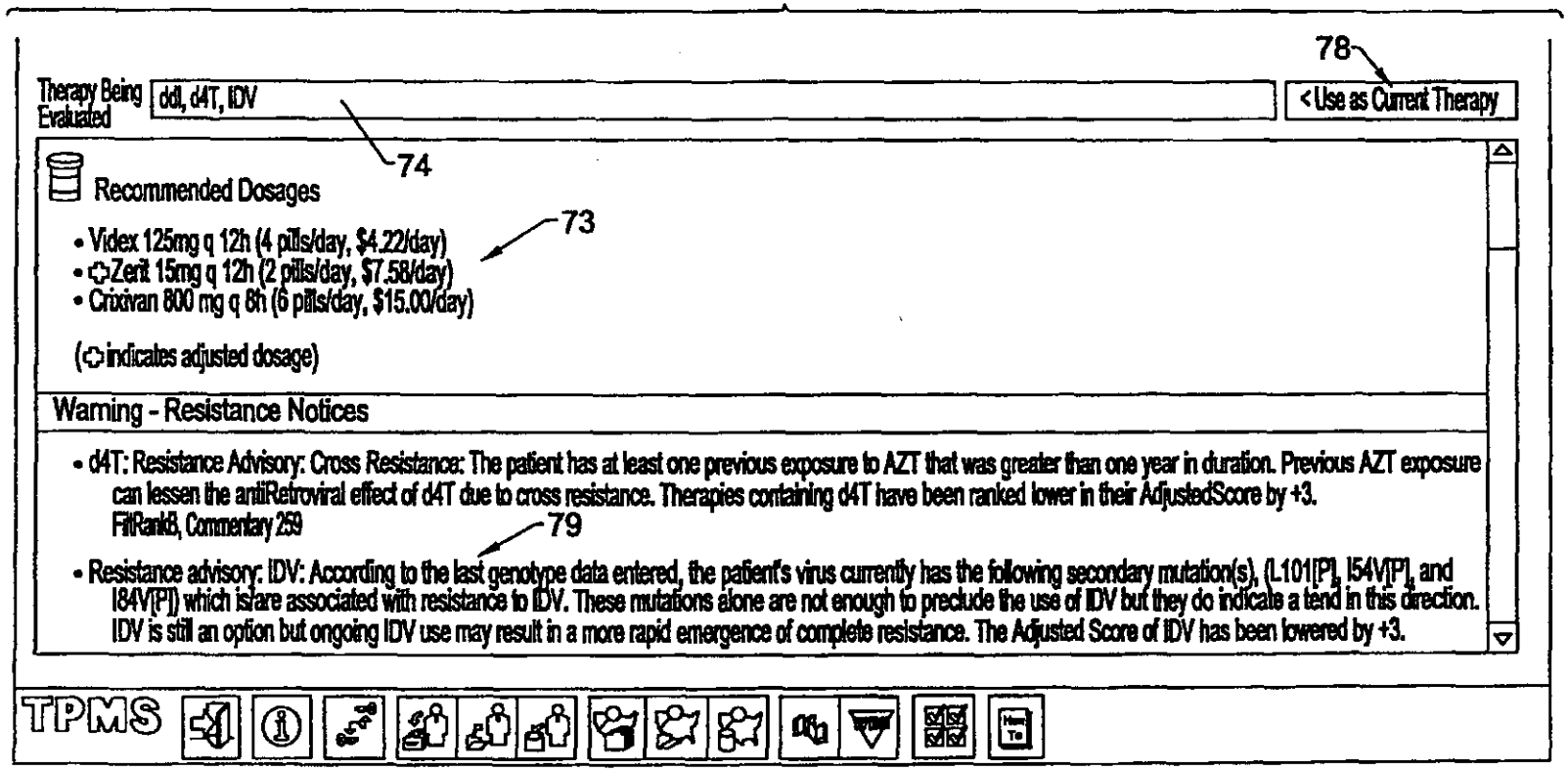


FIG. 6B.

Icon	Meaning
○	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box.
ⓘ	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box. The book indicates that therapy has been studied and a reference is available to review.
△	Indicates a yellow alert. There is important information about this therapy that must be reviewed.
⚠	Indicates a yellow alert. There is important information about this therapy that must be reviewed. The book indicates that therapy has been studied and a reference is available to review.
!	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this therapy to be considered.
! ⓘ	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this thereapy to be considered. The book indicates that therapy has been studied and a reference is available to review.
X	Indicates the therapy is not recommended.

FIG. 7.

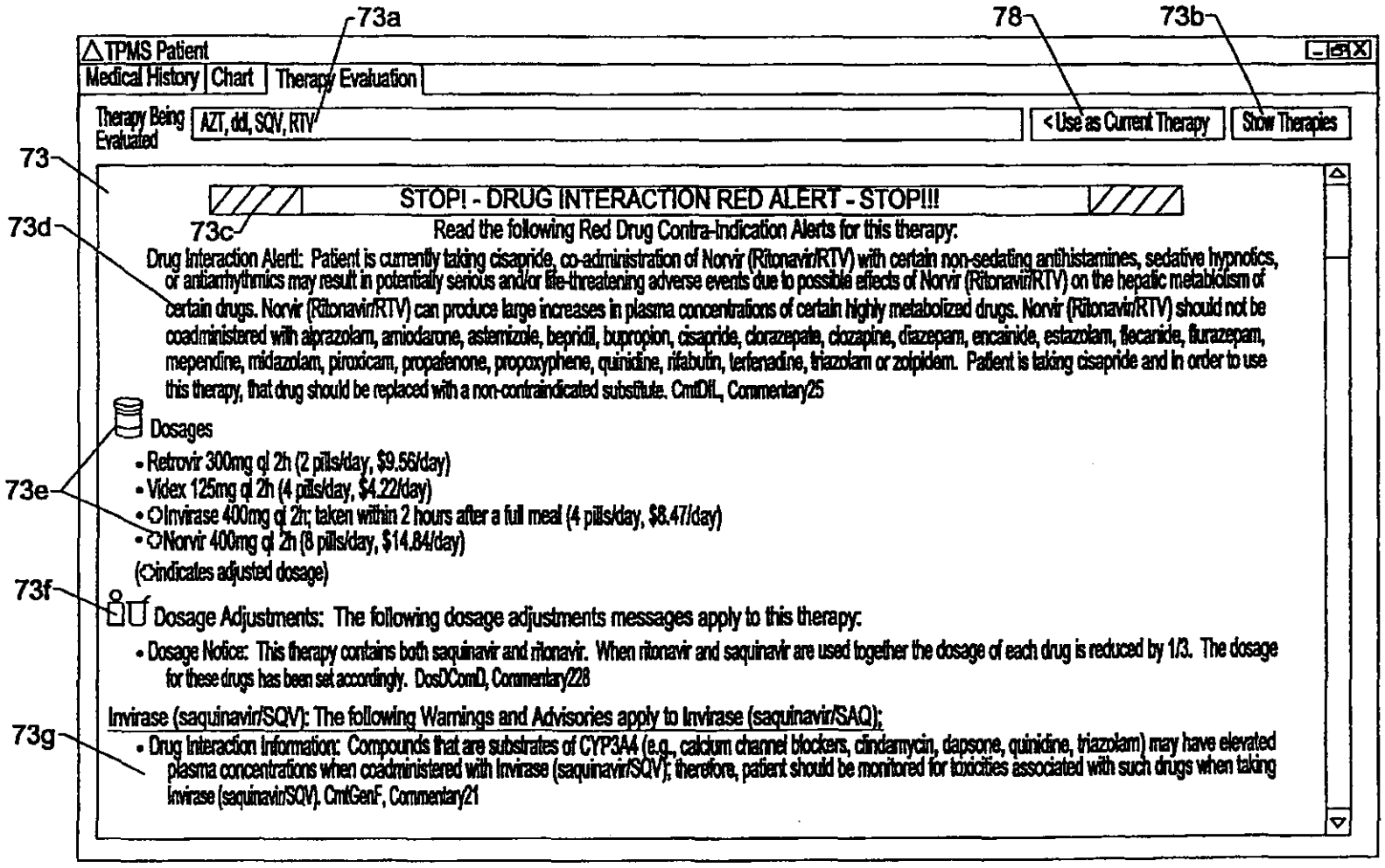

73a
78
73b
TPMS Patient
Medical History
Chart
Therapy Evaluation
Therapy Being Evaluated
AZT, ddI, SQV, RTV
< Use as Current Therapy
Show Therapies
73
73d
73c
STOP! - DRUG INTERACTION RED ALERT - STOP!!!
Read the following Red Drug Contra-Indication Alerts for this therapy:
Drug Interaction Alert!: Patient is currently taking cisapride, co-administration of Norvir (Ritonavir/RTV) with certain non-sedating antihistamines, sedative hypnotics, or antiarrhythmics may result in potentially serious and/or life-threatening adverse events due to possible effects of Norvir (Ritonavir/RTV) on the hepatic metabolism of certain drugs. Norvir (Ritonavir/RTV) can produce large increases in plasma concentrations of certain highly metabolized drugs. Norvir (Ritonavir/RTV) should not be coadministered with alprazolam, amiodarone, astemizole, bepridil, bupropion, cisapride, clorazepate, clozapine, diazepam, encainide, estazolam, flecanide, flurazepam, mependine, midazolam, piroxicam, propafenone, propoxyphene, quinidine, rifabutin, terfenadine, triazolam or zolpidem. Patient is taking cisapride and in order to use this therapy, that drug should be replaced with a non-contraindicated substitute. CmtDil_, Commentary25
73e
Dosages
• Retrovir 300mg ql 2h (2 pills/day, $9.56/day)
• Videx 125mg ql 2h (4 pills/day, $4.22/day)
• ○Invirase 400mg ql 2h; taken within 2 hours after a full meal (4 pills/day, $8.47/day)
• ○Norvir 400mg ql 2h (8 pills/day, $14.84/day)
(○indicates adjusted dosage)
73f
Dosage Adjustments: The following dosage adjustments messages apply to this therapy:
• Dosage Notice: This therapy contains both saquinavir and ritonavir. When ritonavir and saquinavir are used together the dosage of each drug is reduced by 1/3. The dosage for these drugs has been set accordingly. DosDComD, Commentary228
Invirase (saquinavir/SQV): The following Warnings and Advisories apply to Invirase (saquinavir/SAQ):
73g
• Drug Interaction Information: Compounds that are substrates of CYP3A4 (e.g., calcium channel blockers, clindamycin, dapsone, quinidine, triazolam) may have elevated plasma concentrations when coadministered with Invirase (saquinavir/SQV); therefore, patient should be monitored for toxicities associated with such drugs when taking Invirase (saquinavir/SQV). CmtGenF, Commentary21

FIG. 8.

A 110

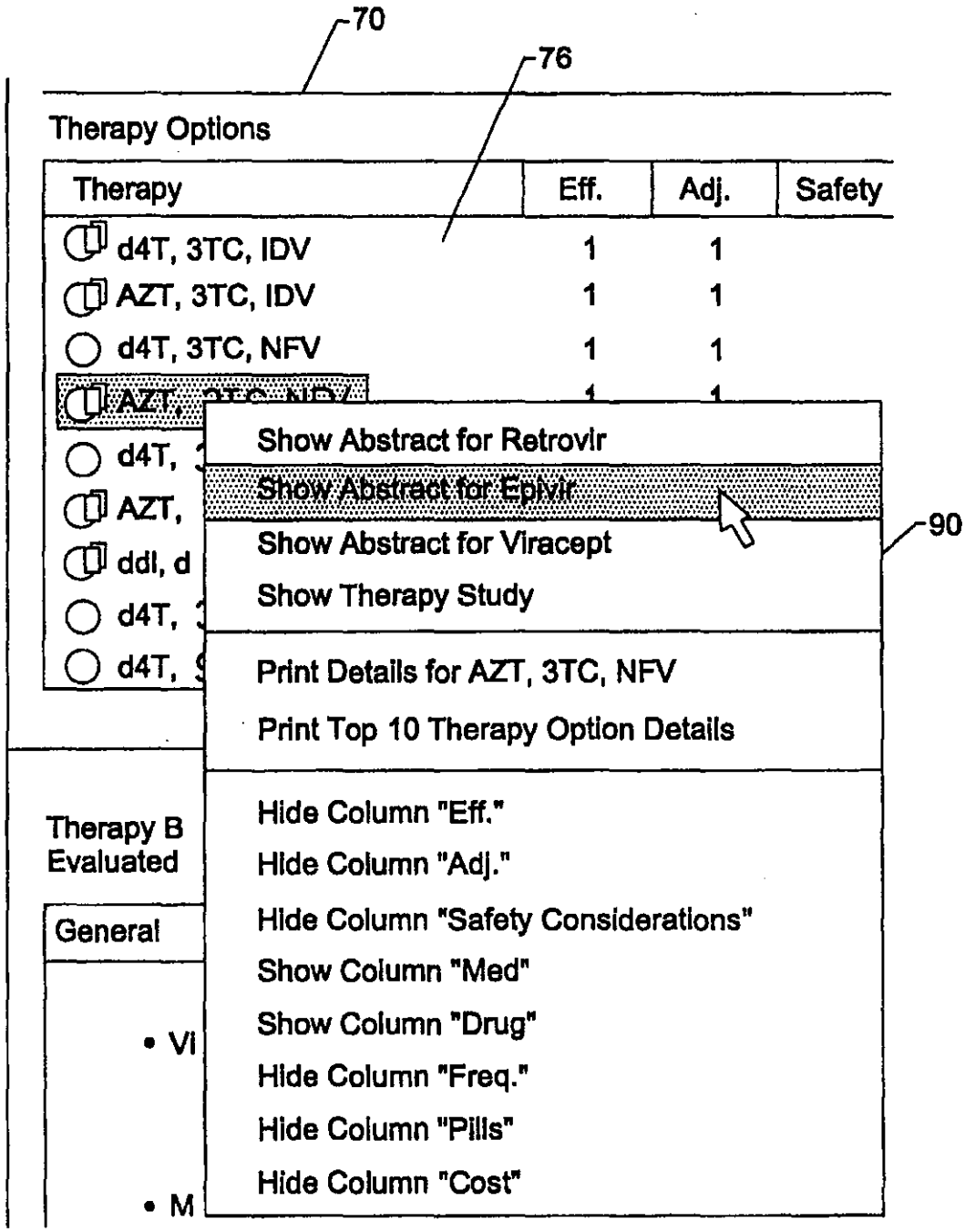

70
76
Therapy Options
Therapy
Eff.
Adj.
Safety
d4T, 3TC, IDV 1 1
AZT, 3TC, IDV 1 1
d4T, 3TC, NFV 1 1
Show Abstract for Retrovir
Show Abstract for Epivir
Show Abstract for Viracept
Show Therapy Study
90
Print Details for AZT, 3TC, NFV
Print Top 10 Therapy Option Details
Therapy B Evaluated
General
Hide Column "Eff."
Hide Column "Adj."
Hide Column "Safety Considerations"
Show Column "Med"
Show Column "Drug"
Hide Column "Freq."
Hide Column "Pills"
Hide Column "Cost"

FIG. 9.

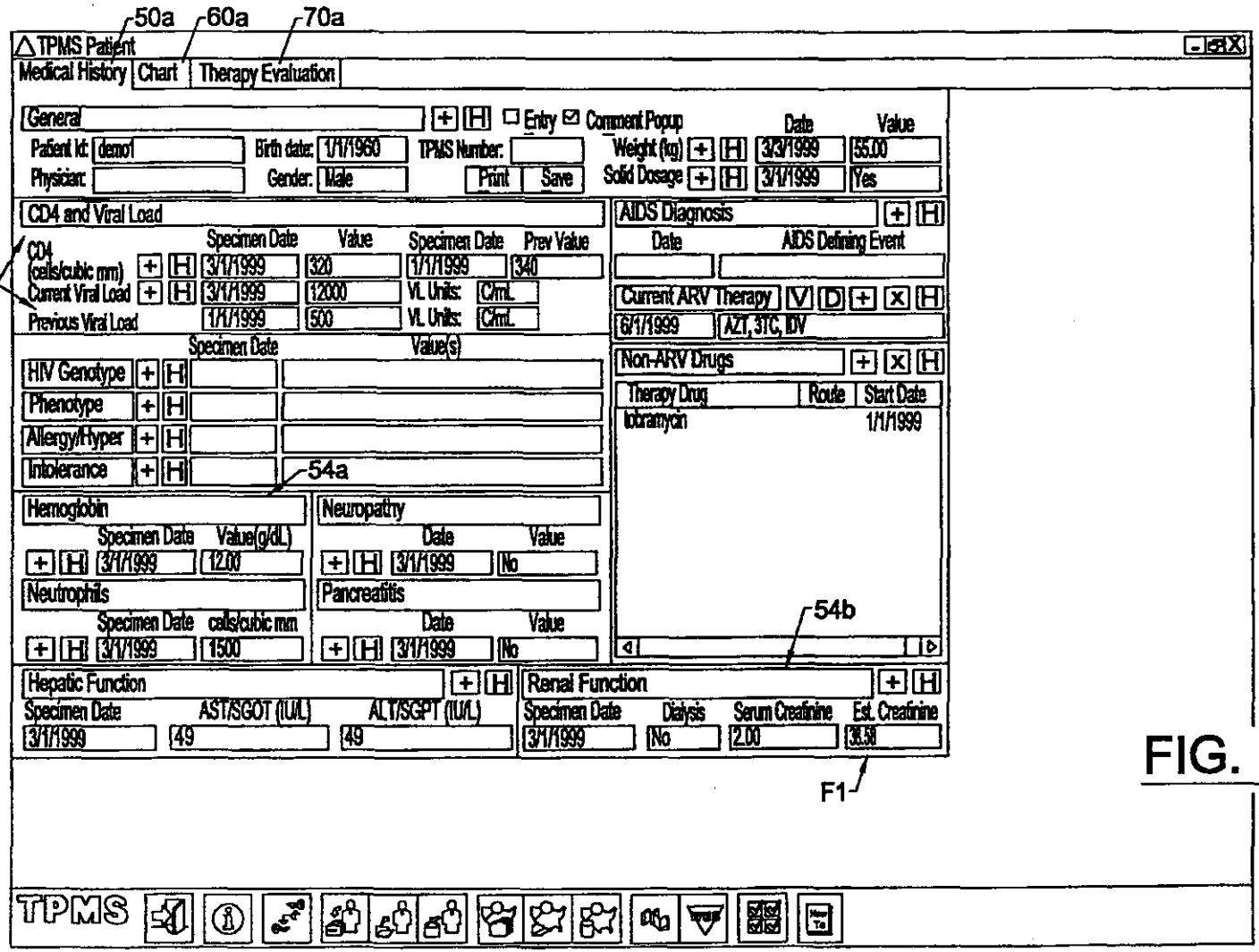

50a
60a
70a
50
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Patient Id: demo1
Birth date: 1/1/1960
TPMS Number:
Physician:
Gender: Male
Print
Save
Weight (kg) 3/3/1999 55.00
Solid Dosage 3/1/1999 Yes
CD4 and Viral Load
Specimen Date
Value
Prev Value
CD4 (cells/cubic mm) 3/1/1999 320 1/1/1999 340
Current Viral Load 3/1/1999 12000 VL Units: Cfml.
Previous Viral Load 1/1/1999 500 VL Units: Cfml.
F2
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Value(s)
54a
AIDS Diagnosis
Date
AIDS Defining Event
Current ARV Therapy
6/1/1999 AZT, 3TC, IDV
Non-ARV Drugs
Therapy Drug
Route
Start Date
tobramycin 1/1/1999
Hemoglobin
Specimen Date
Value(g/dL) 3/1/1999 12.00
Neuropathy
Date
Value 3/1/1999 No
Neutrophils
Specimen Date
cells/cubic mm 3/1/1999 1500
Pancreatitis
Date
Value 3/1/1999 No
54b
Hepatic Function
Specimen Date
AST/SGOT (IU/L) 3/1/1999 49
ALT/SGPT (IU/L) 49
Renal Function
Specimen Date
Dialysis
Serum Creatinine 3/1/1999 No 2.00
Est. Creatinine 38.58
F1
TPMS

FIG. 10A.

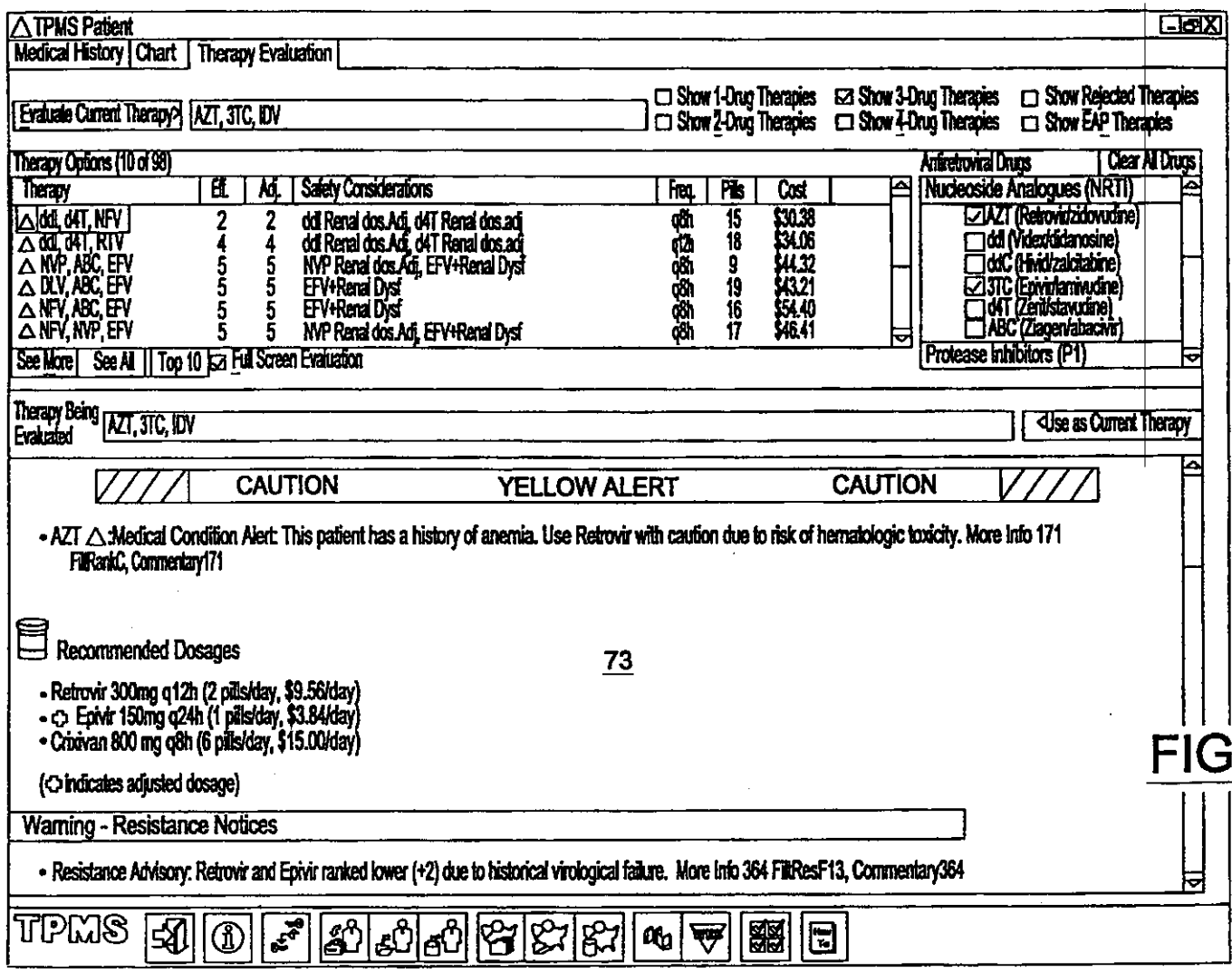

△TPMS Patient
Medical History
Chart
Therapy Evaluation
Evaluate Current Therapy?
AZT, 3TC, IDV
Show 1-Drug Therapies
Show 2-Drug Therapies
Show 3-Drug Therapies
Show 4-Drug Therapies
Show Rejected Therapies
Show EAP Therapies
70
Therapy Options (10 of 98)
Therapy
Eff.
Adj.
Safety Considerations
Freq.
Pills
Cost
△ddI, d4T, NFV 2 2 ddI Renal dos.Adj, d4T Renal dos.adj q8h 15 $30.38
△ddI, d4T, RTV 4 4 ddI Renal dos.Adj, d4T Renal dos.adj q12h 18 $34.06
△NVP, ABC, EFV 5 5 NVP Renal dos.Adj, EFV+Renal Dysf q8h 9 $44.32
△DLV, ABC, EFV 5 5 EFV+Renal Dysf q8h 19 $43.21
△NFV, ABC, EFV 5 5 EFV+Renal Dysf q8h 16 $54.40
△NFV, NVP, EFV 5 5 NVP Renal dos.Adj, EFV+Renal Dysf q8h 17 $46.41
See More
See All
Top 10
Full Screen Evaluation
Antiretroviral Drugs
Clear All Drugs
Nucleoside Analogues (NRTI)
AZT (Retrovir/zidovudine)
ddI (Videx/didanosine)
ddC (Hivid/zalcitabine)
3TC (Epivir/lamivudine)
d4T (Zerit/stavudine)
ABC (Ziagen/abacavir)
Protease Inhibitors (P1)
Therapy Being Evaluated
AZT, 3TC, IDV
Use as Current Therapy
CAUTION
YELLOW ALERT
CAUTION
• AZT △Medical Condition Alert: This patient has a history of anemia. Use Retrovir with caution due to risk of hematologic toxicity. More Info 171 FillRankC, Commentary171
Recommended Dosages
73
• Retrovir 300mg q12h (2 pills/day, $9.56/day)
• ◌ Epivir 150mg q24h (1 pills/day, $3.84/day)
• Crixivan 800 mg q8h (6 pills/day, $15.00/day)
(◌ indicates adjusted dosage)
Warning - Resistance Notices
• Resistance Advisory: Retrovir and Epivir ranked lower (+2) due to historical virological failure. More Info 364 FillResF13, Commentary364
TPMS

FIG. 10B.

A 113

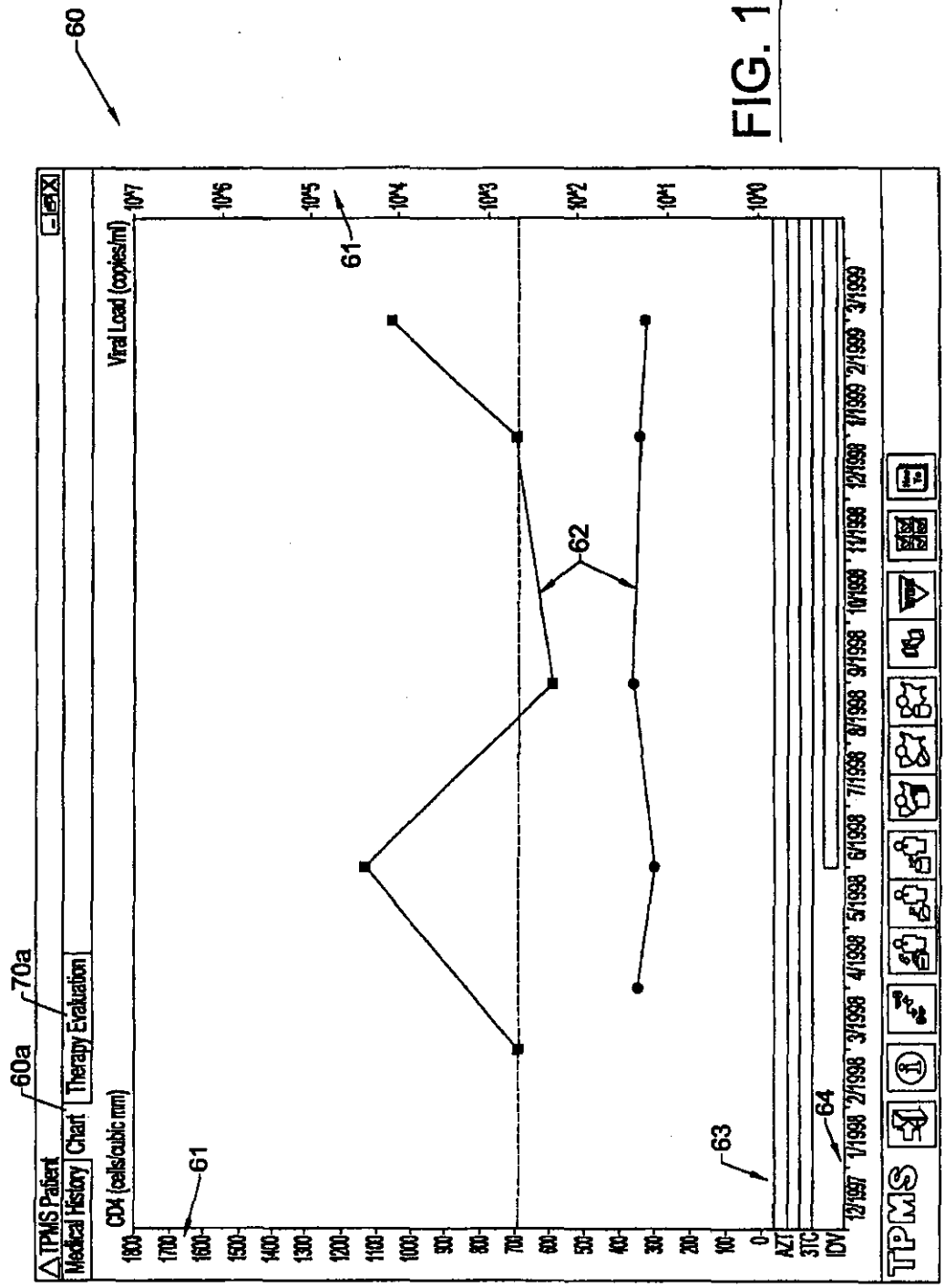

60
60a
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
CD4 (cells/cubic mm)
Viral Load (copies/ml)
61
62
63
64
AZT
3TC
IDV
TPMS

FIG. 10C.

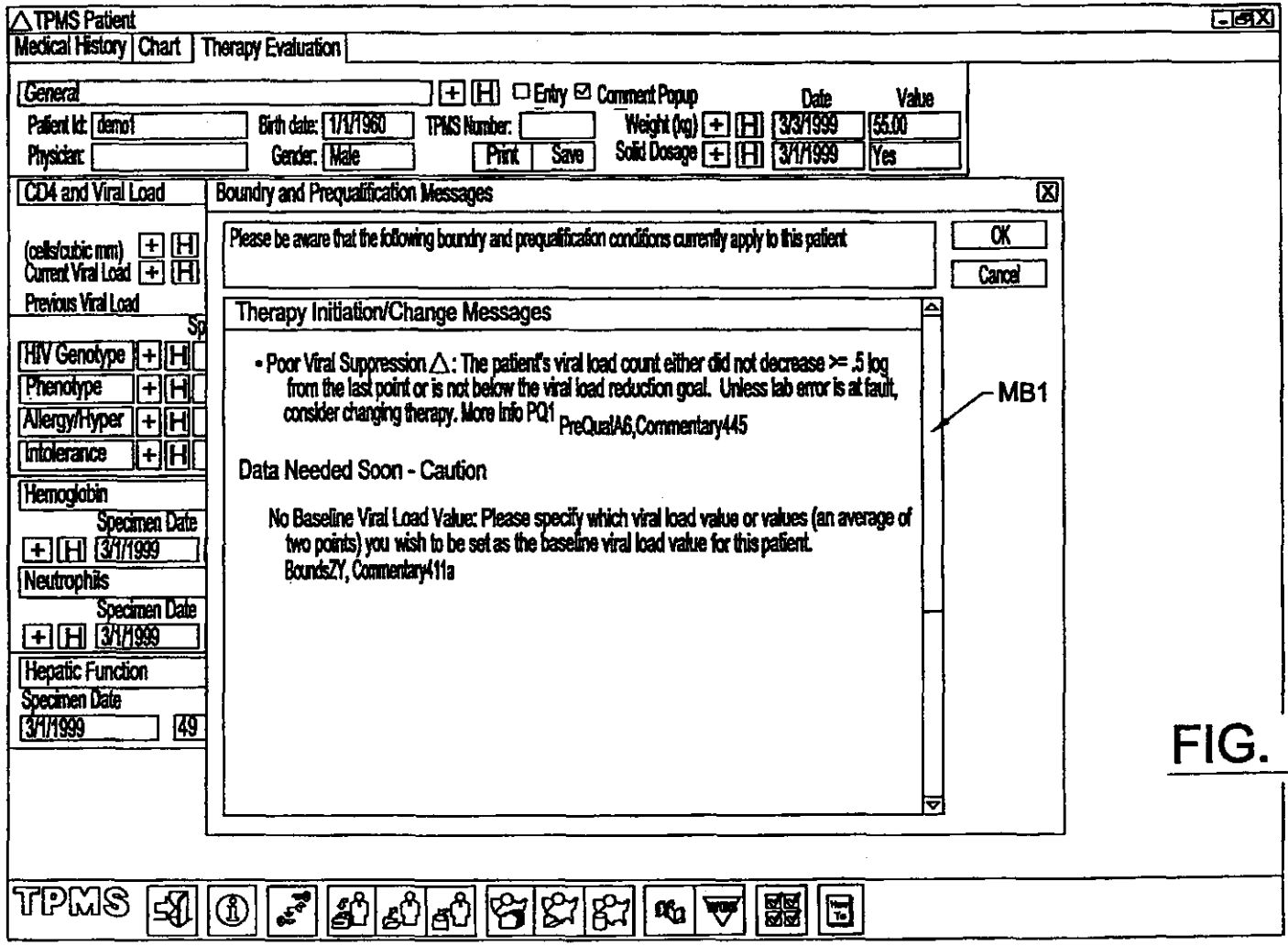

TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Date
Value
Patient Id: demo1
Birth date: 1/1/1960
TPMS Number:
Weight (kg)
3/3/1999
55.00
Physician:
Gender: Male
Print
Save
Solid Dosage
3/1/1999
Yes
CD4 and Viral Load
(cells/cubic mm)
Current Viral Load
Previous Viral Load
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Hemoglobin
Specimen Date
3/1/1999
Neutrophils
Specimen Date
3/1/1999
Hepatic Function
Specimen Date
3/1/1999
49
Boundry and Prequalification Messages
Please be aware that the following boundry and prequalification conditions currently apply to this patient
OK
Cancel
Therapy Initiation/Change Messages
• Poor Viral Suppression △: The patient's viral load count either did not decrease >= .5 log from the last point or is not below the viral load reduction goal. Unless lab error is at fault, consider changing therapy. More Info PQ1 PreQualA6,Commentary445
Data Needed Soon - Caution
No Baseline Viral Load Value: Please specify which viral load value or values (an average of two points) you wish to be set as the baseline viral load value for this patient.
BoundsZY, Commentary411a
TPMS
70
MB1

FIG. 10D.

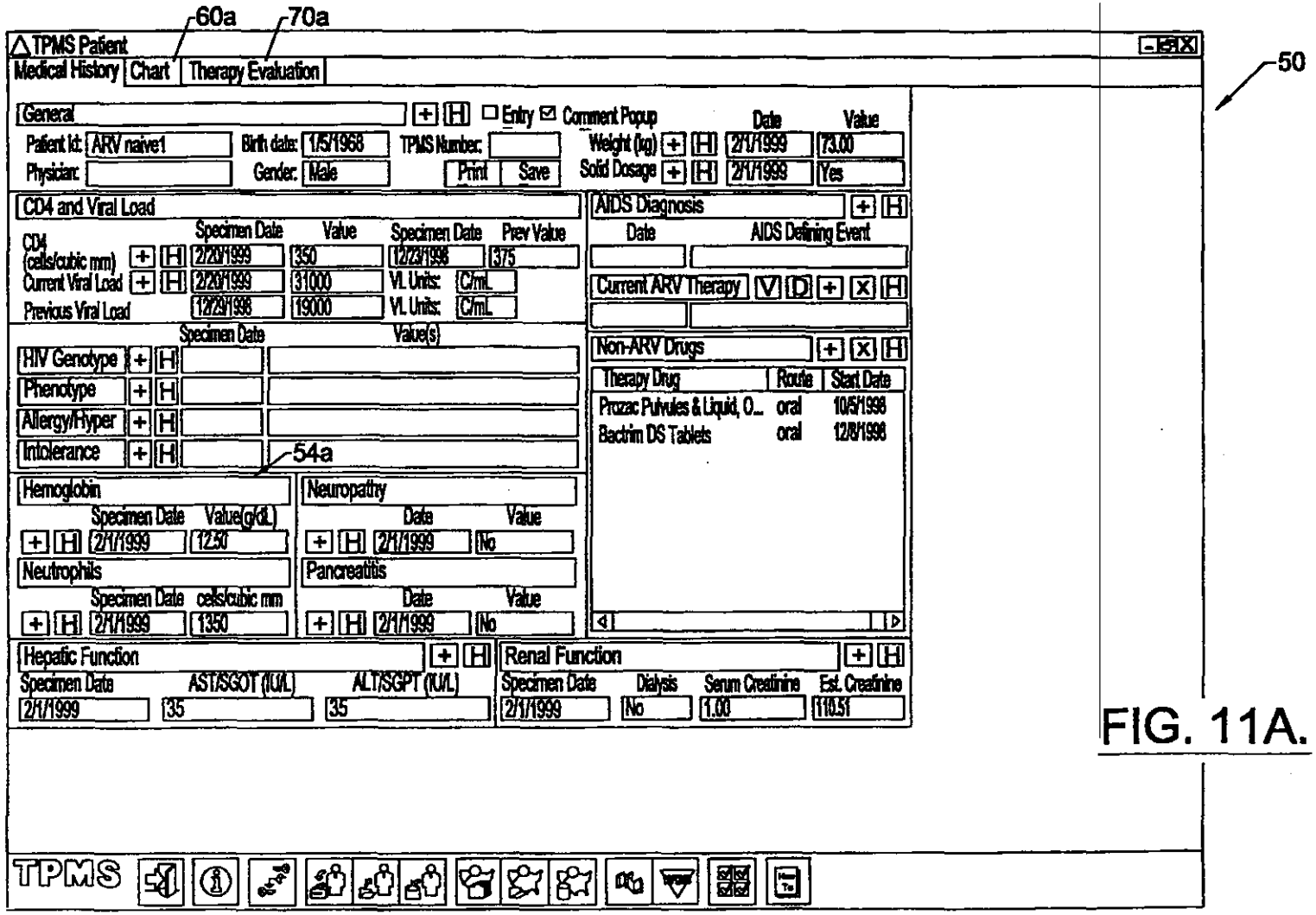

60a
70a
50
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Patient Id: ARV naive1
Birth date: 1/5/1968
TPMS Number:
Physician:
Gender: Male
Print
Save
Weight (kg) 2/1/1999 73.00
Solid Dosage 2/1/1999 Yes
CD4 and Viral Load
Specimen Date
Value
Prev Value
CD4 (cells/cubic mm) 2/20/1999 350 12/29/1998 375
Current Viral Load 2/20/1999 31000 VL Units: C/mL
Previous Viral Load 12/29/1998 19000 VL Units: C/mL
AIDS Diagnosis
Date
AIDS Defining Event
Current ARV Therapy
Non-ARV Drugs
Therapy Drug
Route
Start Date
Prozac Pulvules & Liquid, 0... oral 10/5/1998
Bactrim DS Tablets oral 12/8/1998
Specimen Date
Value(s)
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
54a
Hemoglobin
Specimen Date
Value(g/dL)
2/1/1999 12.50
Neuropathy
Date
Value
2/1/1999 No
Neutrophils
Specimen Date
cells/cubic mm
2/1/1999 1350
Pancreatitis
Date
Value
2/1/1999 No
Hepatic Function
Specimen Date
AST/SGOT (IU/L)
ALT/SGPT (IU/L)
2/1/1999 35 35
Renal Function
Specimen Date
Dialysis
Serum Creatinine
Est. Creatinine
2/1/1999 No 1.00 110.51
TPMS

FIG. 11A.

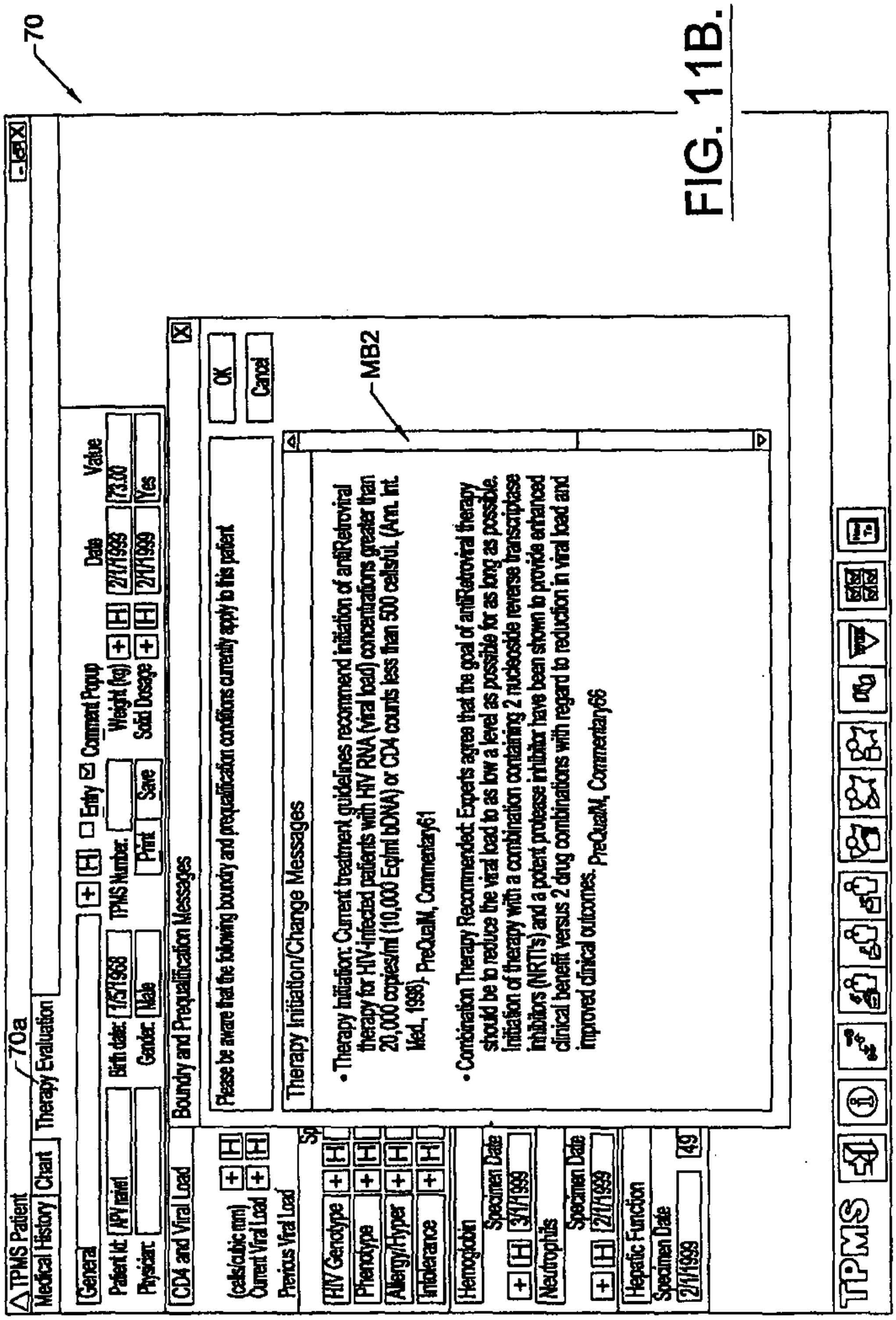

70
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Patient Id: HIV naive
Physician:
Birth date: 1/5/1968
Gender: Male
TPMS Number:
Entry
Comment Popup
Weight (kg)
Solid Dosage
Date
Value
2/1/1999
73.00
Yes
Print
Save
CD4 and Viral Load
(cells/cubic mm)
Current Viral Load
Previous Viral Load
HIV Genotype
Phenotype
Allergy/Hyper
Intolerance
Hemoglobin
Specimen Date
3/1/1999
Neutrophils
2/1/1999
Hepatic Function
2/1/1999
49
Boundry and Prequalification Messages
Please be aware that the following boundry and prequalification conditions currently apply to this patient
OK
Cancel
Therapy Initiation/Change Messages
MB2
• Therapy Initiation: Current treatment guidelines recommend initiation of antiRetroviral therapy for HIV-infected patients with HIV RNA (viral load) concentrations greater than 20,000 copies/ml (10,000 Eq/ml bDNA) or CD4 counts less than 500 cells/uL (Ann. Int. Med., 1998). PreQualM, Commentary61
• Combination Therapy Recommended: Experts agree that the goal of antiRetroviral therapy should be to reduce the viral load to as low a level as possible for as long as possible. Initiation of therapy with a combination containing 2 nucleoside reverse transcriptase inhibitors (NRTI's) and a potent protease inhibitor have been shown to provide enhanced clinical benefit versus 2 drug combinations with regard to reduction in viral load and improved clinical outcomes. PreQualM, Commentary66
TPMS

FIG. 11B.

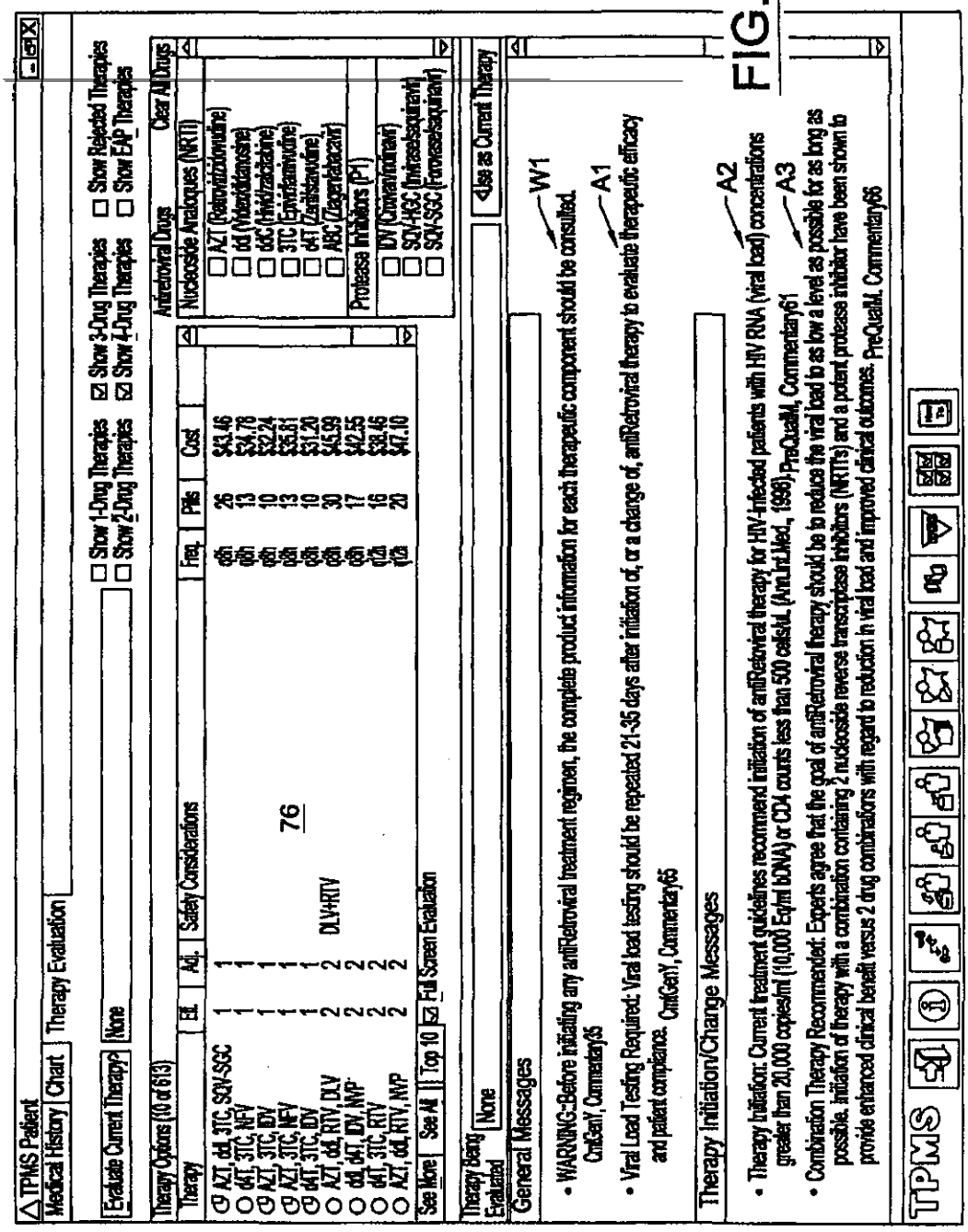


FIG. 11C.

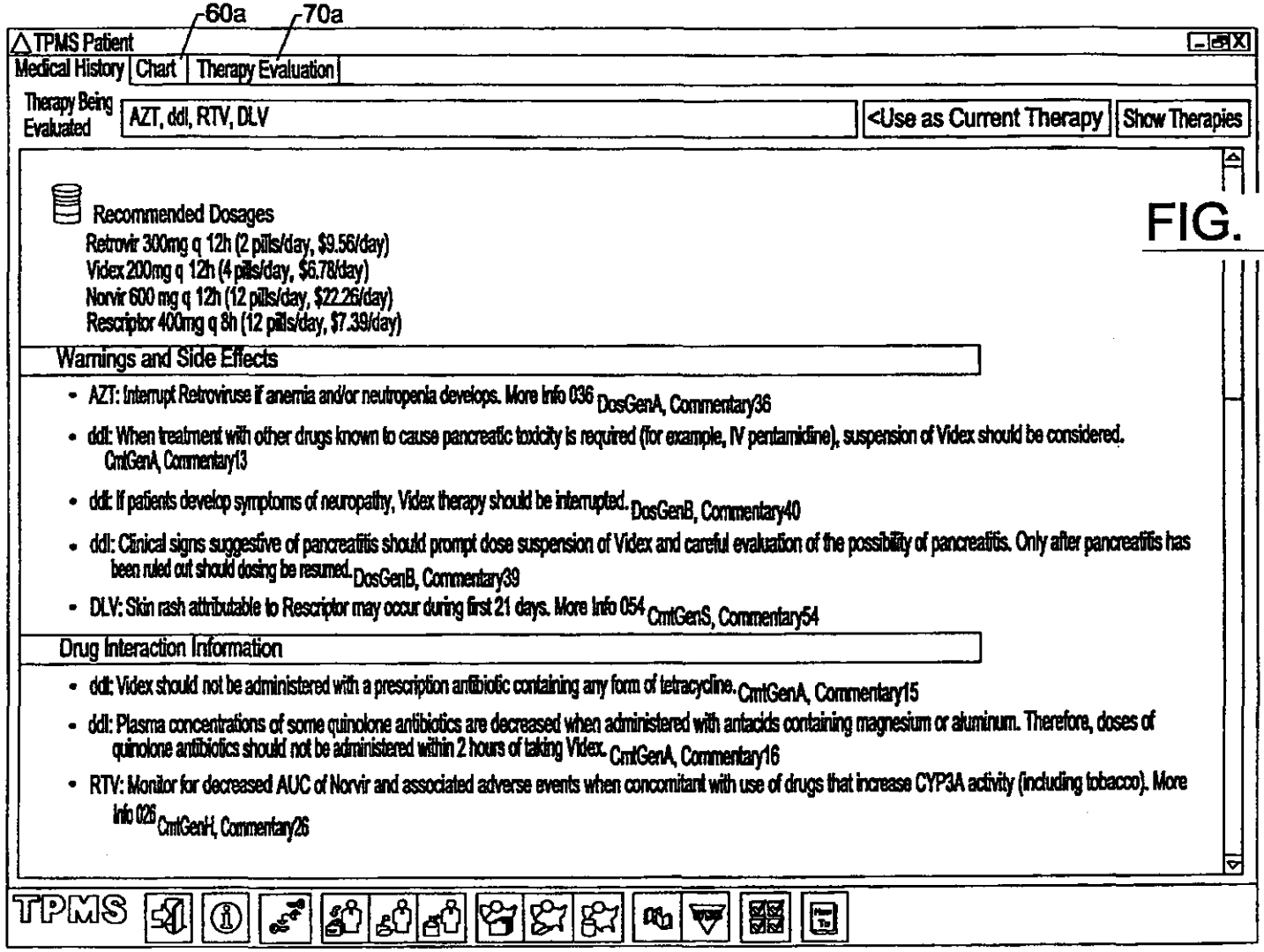

60a
70a
TPMS Patient
Medical History
Chart
Therapy Evaluation
Therapy Being Evaluated
AZT, ddI, RTV, DLV
<Use as Current Therapy
Show Therapies
Recommended Dosages
Retrovir 300mg q 12h (2 pills/day, $9.56/day)
Videx 200mg q 12h (4 pills/day, $6.78/day)
Norvir 600 mg q 12h (12 pills/day, $22.26/day)
Rescriptor 400mg q 8h (12 pills/day, $7.39/day)
Warnings and Side Effects
• AZT: Interrupt Retroviruse if anemia and/or neutropenia develops. More Info 036 DosGenA, Commentary36
• ddI: When treatment with other drugs known to cause pancreatic toxicity is required (for example, IV pentamidine), suspension of Videx should be considered. CmtGenA, Commentary13
• ddI: If patients develop symptoms of neuropathy, Videx therapy should be interrupted. DosGenB, Commentary40
• ddI: Clinical signs suggestive of pancreatitis should prompt dose suspension of Videx and careful evaluation of the possibility of pancreatitis. Only after pancreatitis has been ruled out should dosing be resumed. DosGenB, Commentary39
• DLV: Skin rash attributable to Rescriptor may occur during first 21 days. More Info 054 CmtGenS, Commentary54
Drug Interaction Information
• ddI: Videx should not be administered with a prescription antibiotic containing any form of tetracycline. CmtGenA, Commentary15
• ddI: Plasma concentrations of some quinolone antibiotics are decreased when administered with antacids containing magnesium or aluminum. Therefore, doses of quinolone antibiotics should not be administered within 2 hours of taking Videx. CmtGenA, Commentary16
• RTV: Monitor for decreased AUC of Norvir and associated adverse events when concomitant with use of drugs that increase CYP3A activity (including tobacco). More Info 026 CmtGenH, Commentary26
TPMS

FIG. 11D.

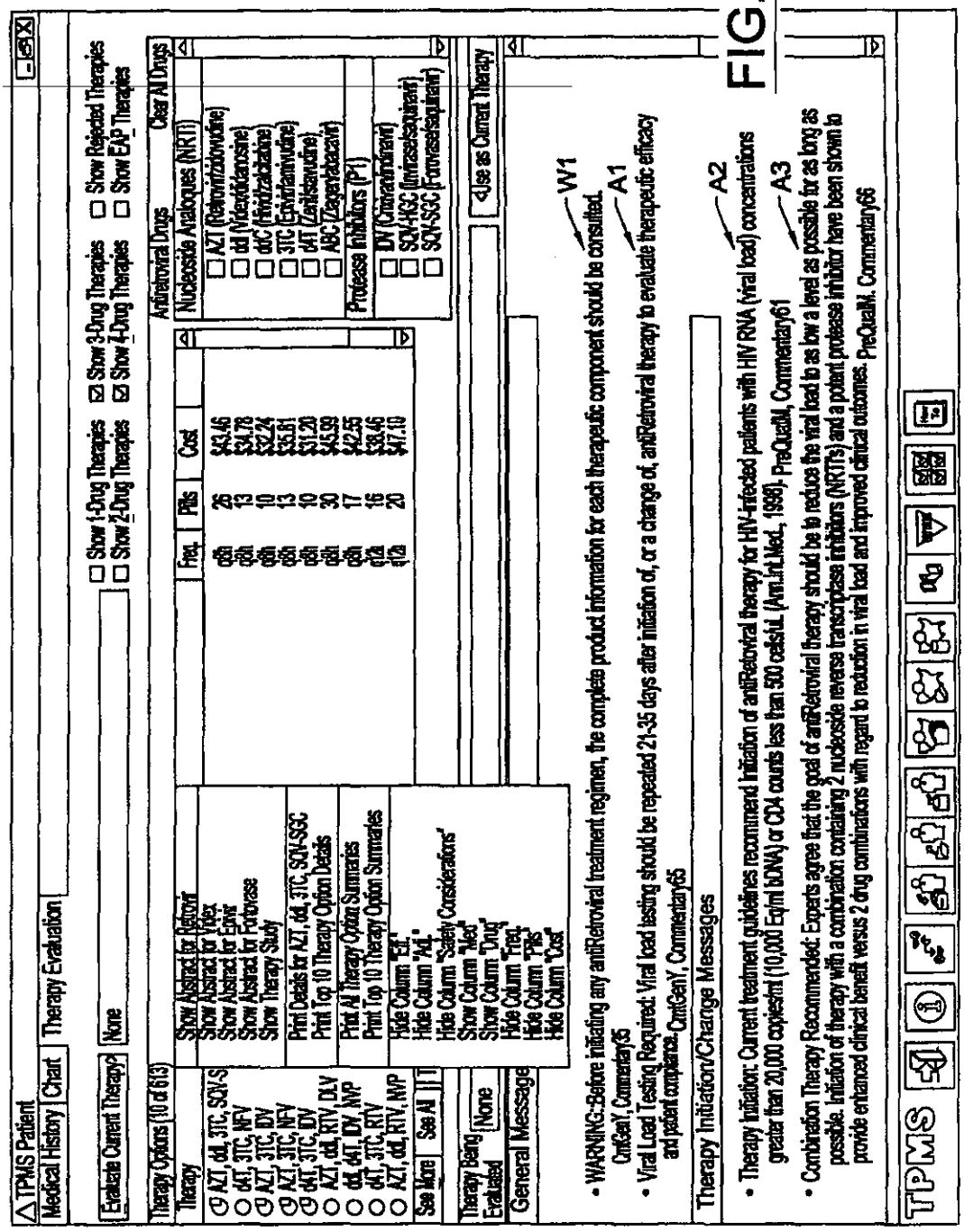


FIG. 11E.

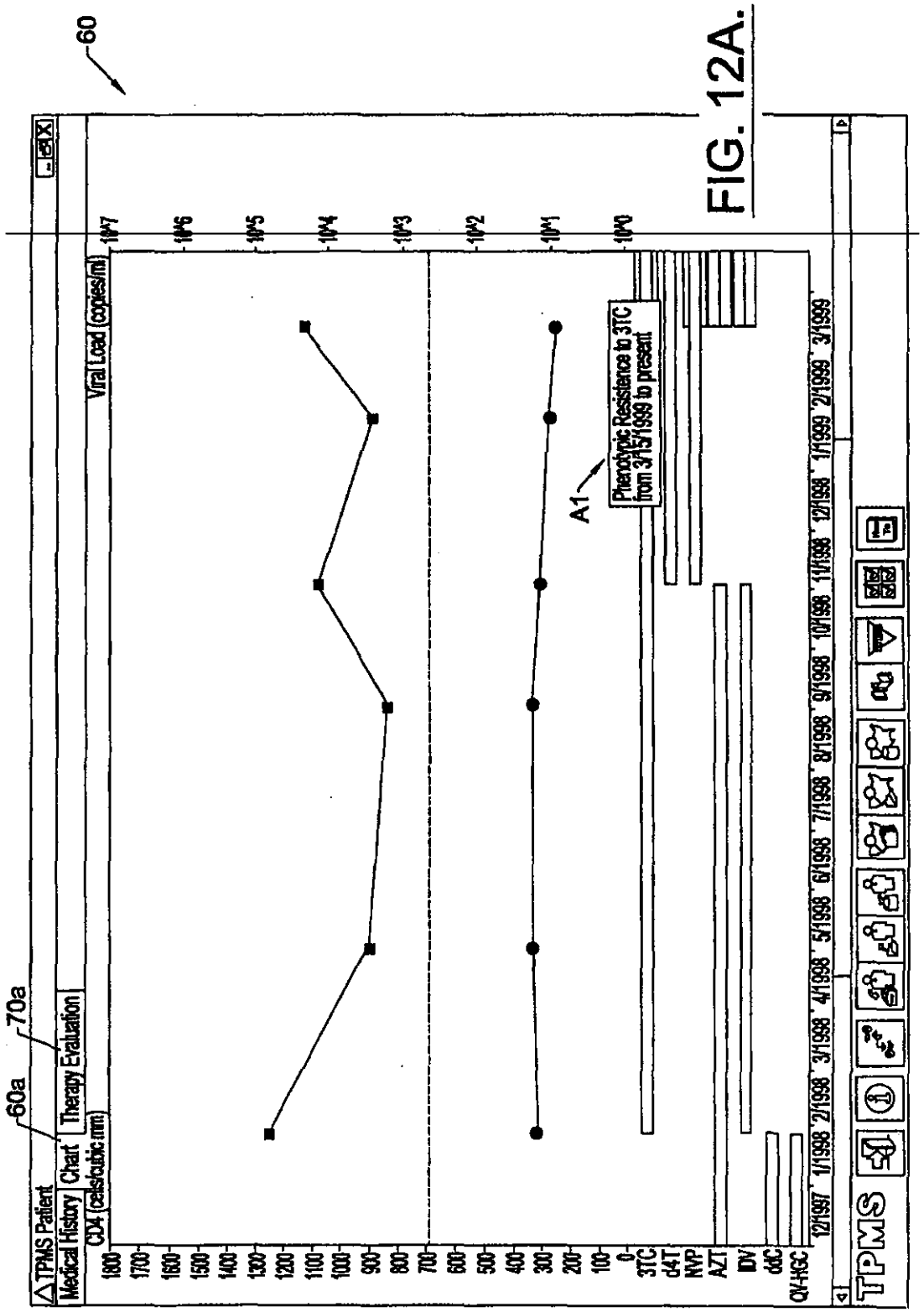


FIG. 12A.

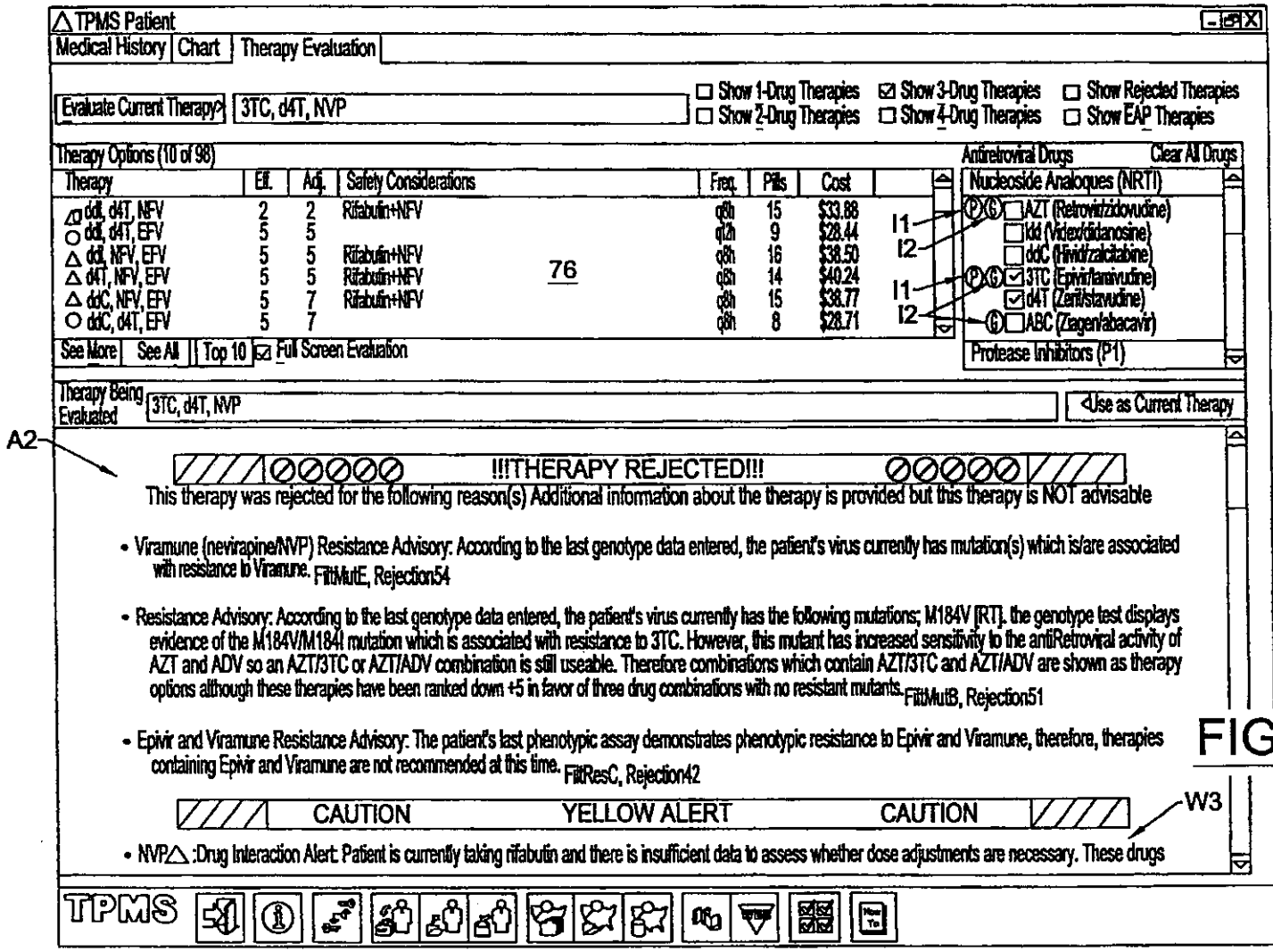

TPMS Patient
Medical History
Chart
Therapy Evaluation
Evaluate Current Therapy?
3TC, d4T, NVP
Show 1-Drug Therapies
Show 2-Drug Therapies
Show 3-Drug Therapies
Show 4-Drug Therapies
Show Rejected Therapies
Show EAP Therapies
Therapy Options (10 of 98)
Therapy
Eff.
Adj.
Safety Considerations
Freq.
Pills
Cost
ddI, d4T, NFV 2 2 Rifabutin+NFV q8h 15 $33.88
ddI, d4T, EFV 5 5 q12h 9 $28.44
ddI, NFV, EFV 5 5 Rifabutin+NFV q8h 16 $38.50
d4T, NFV, EFV 5 5 Rifabutin+NFV q8h 14 $40.24
ddC, NFV, EFV 5 7 Rifabutin+NFV q8h 15 $38.77
ddC, d4T, EFV 5 7 q8h 8 $28.71
I1
I2
I1
I2
76
See More
See All
Top 10
Full Screen Evaluation
Antiretroviral Drugs
Clear All Drugs
Nucleoside Analogues (NRTI)
AZT (Retrovir/zidovudine)
ddI (Videx/didanosine)
ddC (Hivid/zalcitabine)
3TC (Epivir/lamivudine)
d4T (Zerit/stavudine)
ABC (Ziagen/abacavir)
Protease Inhibitors (P1)
Therapy Being Evaluated
3TC, d4T, NVP
Use as Current Therapy
A2
!!!THERAPY REJECTED!!!
This therapy was rejected for the following reason(s) Additional information about the therapy is provided but this therapy is NOT advisable
• Viramune (nevirapine/NVP) Resistance Advisory: According to the last genotype data entered, the patient's virus currently has mutation(s) which is/are associated with resistance to Viramune. FltMutE, Rejection54
• Resistance Advisory: According to the last genotype data entered, the patient's virus currently has the following mutations; M184V [RT]. the genotype test displays evidence of the M184V/M184I mutation which is associated with resistance to 3TC. However, this mutant has increased sensitivity to the antiRetroviral activity of AZT and ADV so an AZT/3TC or AZT/ADV combination is still useable. Therefore combinations which contain AZT/3TC and AZT/ADV are shown as therapy options although these therapies have been ranked down +5 in favor of three drug combinations with no resistant mutants. FltMutB, Rejection51
• Epivir and Viramune Resistance Advisory: The patient's last phenotypic assay demonstrates phenotypic resistance to Epivir and Viramune, therefore, therapies containing Epivir and Viramune are not recommended at this time. FltResC, Rejection42
CAUTION YELLOW ALERT CAUTION
W3
• NVP△ :Drug Interaction Alert: Patient is currently taking rifabutin and there is insufficient data to assess whether dose adjustments are necessary. These drugs
TPMS

FIG. 12B.

A 122

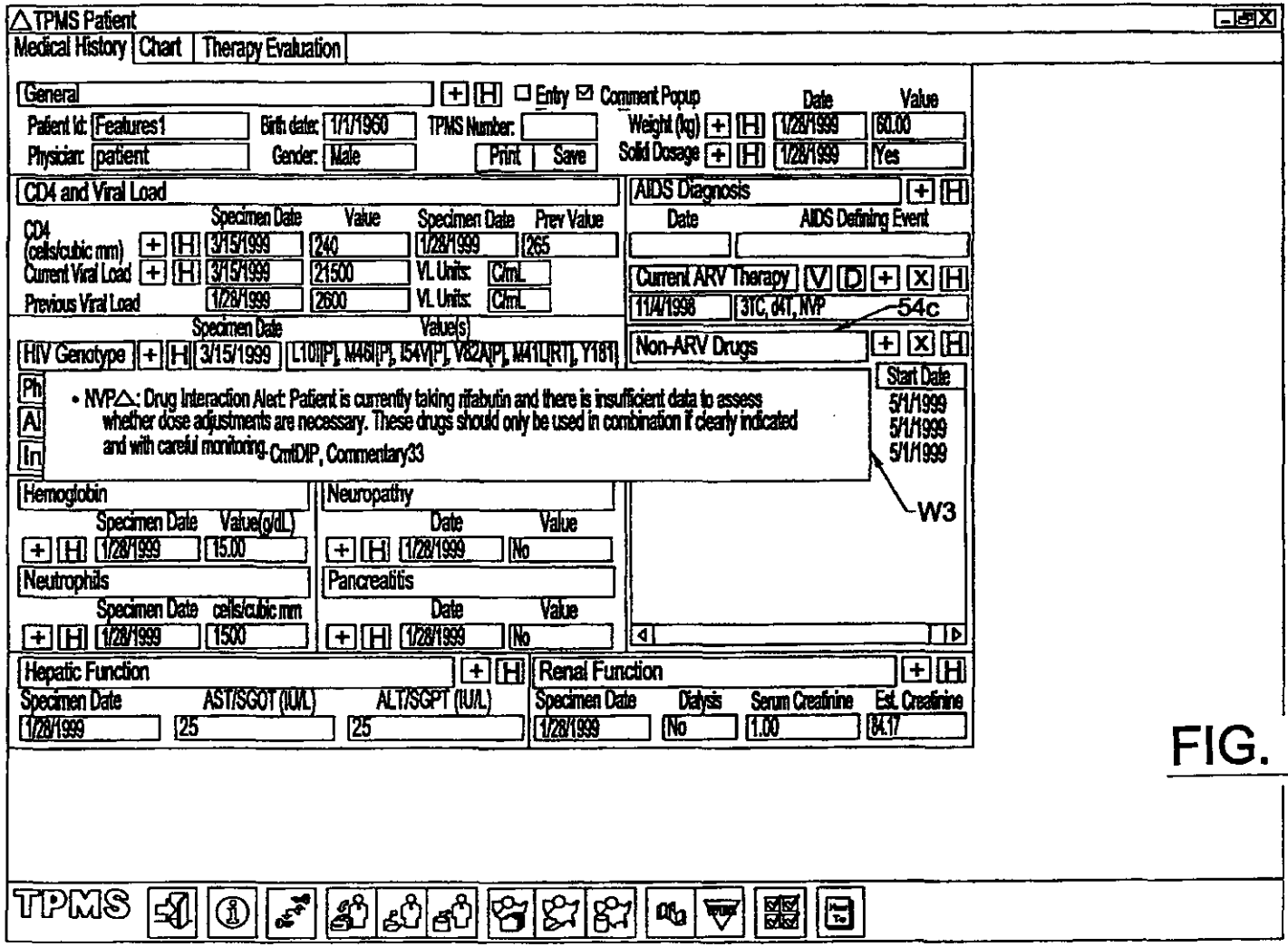

TPMS Patient
Medical History
Chart
Therapy Evaluation
General
Entry
Comment Popup
Patient Id: Features1
Birth date: 1/1/1960
TPMS Number:
Physician: patient
Gender: Male
Print
Save
Weight (kg) 1/28/1999 60.00
Solid Dosage 1/28/1999 Yes
CD4 and Viral Load
CD4 (cells/cubic mm) 3/15/1999 240 1/28/1999 265
Current Viral Load 3/15/1999 21500 VL Units: Cm/L
Previous Viral Load 1/28/1999 2600 VL Units: Cm/L
HIV Genotype 3/15/1999 L10I[P], M46I[P], I54V[P], V82A[P], M41L[RT], Y181
AIDS Diagnosis
Date
AIDS Defining Event
Current ARV Therapy
11/4/1998 3TC, d4T, NVP
54c
Non-ARV Drugs
Start Date
5/1/1999
5/1/1999
5/1/1999
• NVP△: Drug Interaction Alert: Patient is currently taking rifabutin and there is insufficient data to assess whether dose adjustments are necessary. These drugs should only be used in combination if clearly indicated and with careful monitoring. CmtDIP, Commentary33
W3
Hemoglobin
Specimen Date Value(g/dL)
1/28/1999 15.00
Neutrophils
Specimen Date cells/cubic mm
1/28/1999 1500
Neuropathy
Date Value
1/28/1999 No
Pancreatitis
Date Value
1/28/1999 No
Hepatic Function
Specimen Date AST/SGOT (IU/L) ALT/SGPT (IU/L)
1/28/1999 25 25
Renal Function
Specimen Date Dialysis Serum Creatinine Est. Creatinine
1/28/1999 No 1.00 84.17
TPMS

FIG. 12C.

SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS

RELATED APPLICATIONS

This application is a continuation of copending application Ser. No. 09/283,702, filed Apr. 1, 1999, which claims priority from provisional application Ser. No. 60/080,629, filed Apr. 3, 1998, the disclosure of both of which are incorporated by reference herein in their entirety.

FIELD OF THE INVENTION

This invention concerns systems, methods and computer program products for guiding the selection of therapeutic treatment regimens for complex disorders such as cancer and HIV-1 infection, wherein a ranking of available treatment regimens is generated and advisory information clinically useful for treating patients is provided.

BACKGROUND OF THE INVENTION

Therapeutic treatment regimens for disorders such as HIV-1 infection (acquired immune deficiency syndrome or AIDS) and cancer are increasingly complex. New data and new therapeutic treatment regimens continue to modify the treatments available, and it is difficult for all but the specialist to remain current on the latest treatment information. Further, even those who are current on the latest treatment information require time to assimilate that information and understand how it relates to other treatment information in order to provide the best available treatment for a patient. Combination therapeutic treatment regimens exacerbate this problem by making potential drug interactions even more complex. Finally, an increasingly sophisticated patient population, in the face of a vast volume of consumer information on the treatment of disease, makes the mere statement of a treatment regime, without explanation, difficult for the patient to accept.

R. Miller et al., Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems, Ann. Intern. Med. 127, 842–845 (1997), describes policy guidelines indicating the desirability of systems that generate advice for clinician users in a manner that users can easily override. Solutions to this need are neither suggested nor disclosed.

M. Pazzani et al., Application of an Expert System in the Management of HIV-Infected Patients, J. Acquired Immune Deficiency Syndromes and Human Retrovirology 15, 356–362 (1997)(accepted May 12, 1997), describes a rule-based expert system by which protease, reverse transcriptase, and integrase segments of HIV are cloned and entered into an expert system that recommends two, three, and four drug regimens. A means for easily overriding the advice given is neither suggested nor disclosed.

U.S. Pat. No. 5,672,154 to Sillen describes a method for giving patients individualized, situation dependent medication advice. The recommended type of medicine may include at least two different medicines. No means for

ranking multiple treatment options is disclosed, and no means for explaining why treatment options were rejected is given. Rather, this system is primarily concerned with generating new rules from patient information to optimize a particular therapy for diseases such as Parkinson's disease, epilepsy and abnormal blood pressure.

U.S. Pat. No. 5,694,950 to McMichael describes a method and system for use in treating a patient with immunosuppressants such as cyclosporin. An expert system is employed to generate a recommendation on whether the immunosuppressant dosage should be changed and, if so, how. Ranking or selection among a plurality of different combination therapeutic treatment regimens is not suggested.

U.S. Pat. No. 5,594,638 to Iliff describes a medical diagnostic system that provides medical advice to the general public over a telephone network. This system is not concerned with generating a recommendation for a combination therapeutic treatment regimen for a known disease (see also U.S. Pat. No. 5,660,176 to Iliff).

SUMMARY OF THE INVENTION

In view of the foregoing, an object of the invention is to provide systems, methods and computer program products for selecting therapeutic treatment regimens for patients in which available treatments are listed, and optionally ranked, while unavailable or rejected treatment regimens (e.g., regimens that would not be effective, or would be dangerous) are not displayed or are assigned a low rank and are indicated to a user as not likely to be efficacious, or not preferred due to patient-specific complicating factors such as drug interaction from concomitant medications.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the available treatment options can be readily understood.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the implications of selecting a particular treatment regimen can be readily understood.

A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the reasons for rejection of a particular regimen can be readily understood.

A still further object of the invention is to provide systems, methods and computer program products for obtaining information about the efficacy of previous treatment regimens imposed on patients.

A method of the present invention includes providing patient information to a computing device that includes various knowledge bases. For example, a first knowledge base may include a plurality of different therapeutic treatment regimens for a disease or medical condition. A second knowledge base may include a plurality of expert rules for selecting a therapeutic treatment regimen for the disease or medical condition. A third knowledge base may include advisory information useful for the treatment of a patient with different constituents of different therapeutic treatment regimens. A fourth knowledge base may include information about past therapies, such as how a patient has fared under previous therapies.

A listing (preferably a ranked listing) of therapeutic treatment regimens for a patient is generated in the computing device. Advisory information for one or more treatment regimens in the listing is generated in the computing device based on the patient information and the expert rules.

In a preferred embodiment, the method described above further includes entering a user-defined therapeutic treatment regimen for the disease (or medical condition) that may not be displayed from the system knowledge base-generated therapeutic treatment regimens, and generating in the computing device advisory information for the user-defined combination therapeutic treatment regimen.

In addition, in a preferred embodiment, the method described above further includes entering a rejected therapeutic treatment regimen for the disease (or medical condition) that is included in the first knowledge base but not recommended from the ranking (or given a very low ranking), and generating in the computing device advisory information for the non-recommended/low ranked therapeutic treatment regimen, wherein the advisory information includes at least one reason for not recommending (or low ranking) the therapeutic treatment regimen.

Further objects and aspects of the present invention are explained in detail in the drawings herein and the specification set forth below.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate embodiments of the invention and, together with the description, serve to explain principles of the invention.

FIG. 1 illustrates a process of the instant invention, including routines for entering a user-defined therapeutic treatment regimen and for entering a "non-recommended" therapeutic treatment regimen.

FIG. 2 schematically illustrates a system or apparatus of the present invention.

FIG. 3 illustrates a client-server environment within which the system of FIG. 2 may operate, according to an embodiment of the present invention, and wherein a central server is accessible by at least one local server via a computer network, such as the Internet, and wherein each local server is accessible by at least one client.

FIG. 4 illustrates a medical history user interface for entering data about a patient's medical history according to the present invention.

FIG. 5 illustrate a user interface chart for monitoring a patient's condition during a particular therapeutic treatment regimen over a period of time according to the present invention.

FIG. 6 illustrates a therapy evaluation user interface that facilitates evaluation of various therapeutic treatment regimen options with respect to relative efficacy, individualized adjusted relative efficacy, dosage, frequency, cost, medical complications and drug interactions according to the present invention.

FIG. 7 illustrates various symbols for providing information about a therapeutic treatment regimen option within the therapy list box of the therapy evaluation user interface of FIG. 6 according to the present invention.

FIG. 8 illustrates the therapy details box of FIG. 6 in "full screen" mode.

FIG. 9 illustrates a pop-up menu including an indexed electronic link to a PDR® that can be activated from within the therapy list box of the therapy evaluation user interface of FIG. 6 according to the present invention.

FIGS. 10A–10D illustrate various functions of the present invention as described in Example 1.

FIGS. 11A–11E illustrate various functions of the present invention as described in Example 2.

FIGS. 12A–12C illustrate various functions of the present invention as described in Example 3.

DETAILED DESCRIPTION OF THE INVENTION

The present invention now will be described more fully hereinafter with reference to the accompanying drawings, in which preferred embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art. Like numbers refer to like elements throughout.

As will be appreciated by one of skill in the art, the present invention may be embodied as a method, data processing system, or computer program product. Accordingly, the present invention may take the form of an entirely hardware embodiment, an entirely software embodiment, or an embodiment combining software and hardware aspects. Furthermore, the present invention may take the form of a computer program product on a computer-usable storage medium having computer readable program code means embodied in the medium. Any suitable computer readable medium may be utilized including, but not limited to, hard disks, CD-ROMs, optical storage devices, and magnetic storage devices.

The present invention is described below with reference to flowchart illustrations of methods, apparatus (systems), and computer program products according to an embodiment of the invention. It will be understood that each block of the flowchart illustrations, and combinations of blocks in the flowchart illustrations, can be implemented by computer program instructions. These computer program instructions may be provided to a processor of a general purpose computer, special purpose computer, or other programmable data processing apparatus to produce a machine, such that the instructions, which execute via the processor of the computer or other programmable data processing apparatus, create means for implementing the functions specified in the flowchart block or blocks.

These computer program instructions may also be stored in a computer-readable memory that can direct a computer or other programmable data processing apparatus to function in a particular manner, such that the instructions stored in the computer-readable memory produce an article of manufacture including instruction means which implement the function specified in the flowchart block or blocks.

The computer program instructions may also be loaded onto a computer or other programmable data processing apparatus to cause a series of operational steps to be performed on the computer or other programmable apparatus to produce a computer implemented process such that the instructions which execute on the computer or other programmable apparatus provide steps for implementing the functions specified in the flowchart block or blocks.

A method of the instant invention is illustrated in FIG. 1. In the first step 10, the patient is examined to determine patient information. Examples of patient information that may be gathered include one or more of gender, age, weight, $CD4^+$ cell information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, and information for drug treat-

ments for other conditions. The information may include historical information on prior therapeutic treatment regimens for the disease or medical condition. While the patient is typically examined on a first visit to determine the patient information, it will be appreciated that patient information may also be stored in the computing device, or transferred to the computing device from another computing device, storage device, or hard copy, when the information has been previously determined.

The patient information is then provided **11** to a computing device that contains a knowledge base of treatments, contains a knowledge base of expert rules for determining available treatment options for the patient in light of the patient information, and also contains a knowledge base of advisory information. A list of available treatments for the patient is then generated **12** from the patient information and the available treatments by the expert rules, and advisory information for the available treatments is generated **13**. The advisory information may include warnings to take the patient off a contraindicated drug or select a suitable non contraindicated drug to treat the condition before initiating a corresponding treatment regimen and/or information clinically useful to implement a corresponding therapeutic treatment regimen.

For example, when the known disease is HIV-1 infection, the treatment regimen includes antiretroviral drugs, and the treatment regimen or advisory information may also include contraindicated or potentially adversely interacting non-antiretroviral drugs. Particularly, when the treatment regimen includes a protease inhibitor. A contraindicated drug may be terfenadine. When the treatment regimen includes indinavir, a contraindicated drug is cisapride.

Exemplary antiretroviral drugs are listed below in Table 1.

TABLE 1

Abbreviation	Formal Name	Generic Name
ABC	ZIAGEN®	Abacavir
ADV	PREVEON®	Adefovir
APV	AGENERASE®	Amprenavir
AZT	RETROVIR®	Zidovudine
ddI	VIDEX®	Didanosine
ddC	HIVID®	Zalcitabine
d4T	ZERIT®	Stavudine
EFV	SUSTIVA®	Efavirenz
3TC	EPIVIR®	Lamivudine
SQV	INVIRASE®/ FORTOVASE®	Saquinavir
IDV	CRIXIVAN®	Indinavir
RTV	NORVIR®	Ritonavir
DLV	RESCRIPTOR®	Delavirdine
NFV	VIRACEPT®	Nelfinavir
NVP	VIRAMUNE®	Nevirapine

Exemplary advisory information that can be displayed to a user is summarized below in Table 2.

TABLE 2

	Description
Drug Therapies (All the output data types below are associated with a therapy)	The inference engine will process every therapy from a resource file which contains all valid therapy combinations. The system will support multiple drug combinations. Those therapies which are recommended by the knowledge base will be displayed along with all the data types below.
Commentaries	Commentaries consist of warnings and advisories concerning drugs as well as various patient conditions. Each commentary will appear in specific locations of the User Interface. Commentaries will have various Flags, Triggers, and Output Locations.
Rejection Notices	Rejection Notices are the explanation why a given therapy is not recommended. Rejection notices always appear in predefined places in the User Interface.
Cost	The cost per day is calculated for each therapy by the inference engine as well as each drug cost within a therapy.
Dosage	The base dosage and any adjustments to the base dosage due to various patient conditions are calculated by the inference engine.
Pill Burden	The number of pills in the therapy.
Frequency	Number of times the patient will be taking medications for a given therapy. For a multi-drug therapy, the Frequency of the therapy is the drug in the therapy that has the highest number of Frequencies. If a three-drug regimen has 2 drugs with q12h dosages and one that is a q8h, the therapy is considered to be a q8h Frequency.
Admin	Special drug administration instructions.
Efficacy	The relative Efficacy is a whole number that represents the relative efficacy of the various therapies. One is the most effective therapy.
Adjusted Score	The "Adjusted Score" is the Efficacy adjusted up or down based on patient specific characteristics to roughly indicate the likelihood of that therapy being an effective treatment for that patient. An example would be: the system evaluates a therapy containing a drug that is known to be associated with a medical condition in that patient's medical history, therefore the therapy is ranked low. The Ranking Ordinal is an integer, beginning with 0 and having no upper limit. A therapy with a 1 Ranking Ordinal (RO = 1) would be ranked at the top of the list whereas a therapy with a 10 Ranking Ordinal (RO = 10) would be less likely to be successful given the patient's specific history and characteristics. Each therapy will have a starting RO number which will be the therapy's relative efficacy score. The relative efficacy score can then be adjusted up or down by the rules. Both base "Efficacy" number and the "Adjusted Score" number can be displayed.

Diseases (or medical conditions), the treatment of which may be facilitated or improved by the present invention, are those for which multiple different therapy options are available for selection and treatment. Such diseases and medical conditions include, but are not limited to, cardiovascular disease (including but not limited to congestive heart failure, hypertension, hyperlipidemia and angina), pulmonary disease (including but not limited to chronic obstructive pulmonary disease, asthma, pneumonia, cystic fibrosis, and tuberculosis), neurologic disease (including but not limited to Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, amyotrophic lateral sclerosis or ALS, psychoses such as schizophrenia and organic brain syndrome, neuroses, including anxiety, depression and bipolar disorder), hepatitis infections (including hepatitis B and hepatitis C infection), urinary tract infections, venereal disease, cancer (including but not limited to breast, lung, prostate, and colon cancer), etc. It should be appreciated that prevention of development or onset of the above-mentioned diseases and medical conditions may be facilitated or improved by the present invention.

The present invention is useful for known diseases such as HIV-1 infection (acquired immune deficiency syndrome or "AIDS"), or where the known disease is any medical condition for which a combination therapeutic treatment regimen can be used. The invention is particularly useful when the list of available treatments includes a plurality (e.g., 2, 10

or 15 or more) of treatment, combination therapeutic treatment regimens (e.g., therapeutic treatment regimens incorporating two or more active therapeutic agents), where the potential for drug interactions is increased and/or the complexity involved in selecting the best available treatment is multifactorial.

Advantageously, the list of available treatments and advisory information may be regenerated in a number of ways. The patient information may be simply modified **18**. In addition, if a particular therapy in which the user might be interested is not presented, a user-defined therapy may be entered **14** and advisory information generated **15** based on the user-defined therapy. Still further, if a therapeutic treatment regimen that is in the knowledge base is rejected by the system (not recommended upon display), the non-recommended therapeutic treatment regimen may be entered **16** and advisory information generated **17** for the non-recommended therapeutic treatment regimen. This may indicate to the user that they should discontinue use of a non-critical drug for another condition or select a suitable substitute that does not create a conflict/non-recommended situation so that they can then proceed with the therapy of choice. Alternatively, the advisory information can be generated automatically for non-recommended therapeutic treatment regimens. These various steps can be repeated in any sequence in an interactive manner to provide the user with assurance that all treatment options have been given adequate and appropriate consideration.

The terms "therapy" and "therapeutic treatment regimen" are interchangeable herein and, as used herein, mean any pharmaceutical or drug therapy, regardless of the route of delivery (e.g., oral, intraveneous, intramuscular, subcutaneous, intraarterial, intraperitoneal, intrathecal, etc.), for any disease (including both chronic and acute medical conditions, disorders, and the like). In addition, it is understood that the present invention is not limited to facilitating or improving the treatment of diseases. The present invention may be utilized to facilitate or improve the treatment of patients having various medical conditions, without limitation.

System Description

The present invention may be embodied as an expert system that provides decision support to physicians (or other health care providers) treating patients with a known disease, such as HIV infection. A system according to the present invention calculates combination antiretroviral therapy options and attaches all relevant information to those options.

As known to those of skill in the art, an expert system, also known as artificial intelligence (AI), is a computer program that can simulate the judgment and behavior of a human or an organization that has expert knowledge and experience in a particular field. An expert system typically contains a knowledge base containing accumulated experience and a set of rules for applying the knowledge base to each particular situation that is described to the program. Expert systems are well known to those of skill in the art and need not be described further herein.

The antiretroviral therapy options (combinations of antiretroviral drugs), are derived using a knowledge base consisting of a number of expert system rules and functions which in turn take into account a given patient's treatment history, current condition and laboratory values. A system according to the present invention supports the entry, storage, and analysis of patient data in a large central database. A system according to the present invention has a flexible data driven architecture and custom reporting capabilities designed to support patient therapy management and clinical drug trial activities such as screening, patient tracking and support. It is anticipated that a system according to the present invention may be used by health care providers (including physicians), clinical research scientists, and possibly healthcare organizations seeking to find the most cost-effective treatment options for patients while providing the highest standard of care.

A system **20** for carrying out the present invention is schematically illustrated in FIG. **2**. The system **20** comprises a knowledge base of treatment regimens **21**, which may be ranked for efficacy (e.g., by a panel of experts) or ranked according to system rules, a knowledge base of expert rules **22**, a knowledge base of advisory information **23**, a knowledge base of patient therapy history **24** and patient information **25**. Patient information is preferably stored within a database and is configured to be updated. The knowledge bases and patient information **21–25** may be updated by an input/output system **29**, which can comprise a keyboard (and/or mouse) and video monitor. Note also that, while the knowledge bases and patient data **21–25** are shown as separate blocks, the knowledge bases and patient data **21–25** can be combined together (e.g., the expert rules and the advisory information can be combined in a single database).

To carry out the method described above, the information from blocks **21–25** is provided to an inference engine **26**, which generates the listing of available treatments and the corresponding advisory information from the information provided by blocks **21–25**. The inference engine **26** may be implemented as hardware, software, or combinations thereof. Inference engines are known and any of a variety thereof may be used to carry out the present invention. Examples include, but are not limited to, those described in U.S. Pat. No. 5,263,127 to Barabash et al. (Method for fast rule execution of expert systems); U.S. Pat. No. 5,720,009 to Kirk et al. (Method of rule execution in an expert system using equivalence classes to group database objects); U.S. Pat. No. 5,642,471 to Paillet (Production rule filter mechanism and inference engine for expert system); U.S. Pat. No. 5,664,062 to Kim (High performance max-min circuit for a fuzzy inference engine).

High-speed inference engines are preferred so that the results of data entered are continually updated as new data is entered. As with the knowledge bases and patient information in blocks **21–25**, the inference engine **26** may be a separate block from the knowledge bases and patient information blocks **21–25**, or may be combined together in a common program or routine.

Note that the advisory information that is generated for any available therapy may differ from instance to instance based on differences in the patient information provided.

System Architecture

The present invention can be implemented as a system running on a stand alone computing device. Preferably, the present invention is implemented as a system in a client-server environment. As is known to those of skill in the art, a client application is the requesting program in a client-server relationship. A server application is a program that awaits and fulfills requests from client programs in the same or other computers. Client-server environments may include public networks, such as the Internet, and private networks often referred to as "intranets", local area networks (LANs) and wide area networks (WANs), virtual private networks

(VPNs), frame relay or direct telephone connections. It is understood that a client application or server application, including computers hosting client and server applications, or other apparatus configured to execute program code embodied within computer usable media, operates as means for performing the various functions and carries out the methods of the various operations of the present invention.

Referring now to FIG. 3, a client-server environment 30 according to a preferred embodiment of the present invention is illustrated. The illustrated client-server environment 30 includes a central server 32 that is accessible by at least one local server 34 via a computer network 36, such as the Internet. A variety of computer network transport protocols including, but not limited to TCP/IP, can be utilized for communicating between the central server 32 and the local servers 34.

Central Server

The central server 32 includes a central database 38, such as the Microsoft® SQL Server application program, version 6.5 (available from Microsoft, Inc., Redmond, WA), executing thereon. The central server 32 ensures that the local servers 34 are running the most recent version of a knowledge base. The central server 32 also stores all patient data and performs various administrative functions including adding and deleting local servers and users to the system (20, FIG. 2). The central server 32 also provides authorization before a local server 34 can be utilized by a user. Patient data is preferably stored on the central server 32, thereby providing a central repository of patient data. However, it is understood that patient data can be stored on a local server 34 or on local storage media.

Local Server

Each local server 34 typically serves multiple users in a geographical location. Each local server 34 includes a server application, an inference engine, one or more knowledge bases, and a local database 39. Each local server 34 performs artificial intelligence processing for carrying out operations of the present invention. When a user logs on to a local server 34 via a client 35, the user is preferably authenticated via an identification and password, as would be understood by those skilled in the art. Once authenticated, a user is permitted access to the system (20, FIG. 2) and certain administrative privileges are assigned to the user.

Each local server 34 also communicates with the central server 32 to verify that the most up-to-date version of the knowledge base(s) and application are running on the requesting local server 34. If not, the requesting local server 34 downloads from the central server 32 the latest validated knowledge base(s) and/or application before a user session is established. Once a user has logged onto the system (20, FIG. 2) and has established a user session, all data and artificial intelligence processing is preferably performed on a local server 34. An advantage of the illustrated client-server configuration is that most of the computationally intensive work occurs on a local server 34, thereby allowing "thin" clients 35 (i.e., computing devices having minimal hardware) and optimizing system speed.

In a preferred embodiment, each local server database 39 is implemented via a Microsoft® SQL Server application program, Version 6.5. The primary purpose of each local database 39 is to store various patient identifiers and to ensure secure and authorized access to the system (20, FIG. 2) by a user. It is to be understood, however, that both central and local databases 38, 39 may be hosted on the central server 32.

Local Client

Each local client 35 also includes a client application program that consists of a graphical user interface (GUI) and a middle layer program that communicates with a local server 34. Program code for the client application program may execute entirely on a local client 35, or it may execute partly on a local client 35 and partly on a local server 34. As will be described below, a user interacts with the system (20, FIG. 2) by entering (or accessing) patient data within a GUI displayed within the client 35. The client 35 then communicates with a local server 34 for analysis of the displayed patient information.

Computer program code for carrying out operations of the present invention is preferably written in an object oriented programming language such as JAVA®, Smalltalk, or C++. However, the computer program code for carrying out operations of the present invention may also be written in conventional procedural programming languages, such as the "C" programming language, in an interpreted scripting language, such as Perl, or in a functional (or fourth generation) programming language such as Lisp, SML, or Forth.

The middle layer program of the client application includes an inference engine within a local server 34 that provides continuous on-line direction to users, and can instantly warn a user when a patient is assigned drugs or a medical condition that is contraindicated with, or antagonistic of, the patient's current antiretroviral therapy. Every time patient data is entered into the system (20, FIG. 2) or updated, or even as time passes, the inference engine evaluates the current status of the patient data, sorting, categorizing, ranking and customizing every possible antiretroviral therapy for a patient according to the specific needs of the patient.

Inference Engine

Inference engines are well known by those of skill in the art and need not be described further herein. Each knowledge base used by an inference engine according to the present invention is a collection of rules and methods authored by a clinical advisory panel of HIV-treating physicians and scientists. A knowledge base may have subjective rules, objective rules, and system-generated rules. Objective rules are based on industry established facts regarding the treatment of HIV using antiretroviral therapy and are drawn from the package insert information of antiretroviral drug manufacturers and from peer reviewed and published journal articles. An example of an objective rule would be an antiretroviral to antiretroviral contraindication such as:

Rule #1: If the eval therapy contains Zidovudine (AZT) and Stavudine (d4T), then reject the therapy.

In Rule #1, the term "eval therapy" refers to the therapy currently being analyzed by the system (20, FIG. 2). Rule #1 then states that if this therapy contains both AZT and d4T, then this therapy should not be displayed in a list of potential therapy options for the patient.

For objective rules, the present invention can be configured so as to prevent a user from receiving recommendations on new therapy options when certain crucial data on the patient has not been entered. However, it is understood that the present invention does not prevent a health care provider, such as a physician, from recording his/her therapy decisions, even if the system (20, FIG. 2) has shown reasons why that therapy may be harmful to the patient. The present invention allows a health care provider to be the final authority regarding patient therapy.

Subjective rules are based on expert opinions, observations and experience. Subjective rules are typically developed from "best practices" information based on consensus opinion of experts in the field. Such expert opinion may be based on knowledge of the literature published or presented in the field or their own experience from clinical practice, research or clinical trials of approved and unapproved medications. A number of experts are used so that personal bias is reduced.

System generated rules are those derived from the outcomes of patients tracked in the system who received known and defined therapies and either improved, stabilized or worsened during a defined period. Because of the large number of potential combinations usable in HIV infection, this system generated database and rules derived from them are likely to encompass data beyond that achievable from objective or subjective rules databases.

The rules which comprise the various knowledge bases (21–24, FIG. 2) of the present invention each have two main parts: a premise and a conclusion—also referred to as the left side and the right side, respectively. When a premise of a rule is found to be true, the action specified in the conclusion is taken. This is known to those of skill in the art as "firing" the rule. For example, consider the following rule:

Rule ID	Premise	Conclusion
FiltDComAI-	If the eval therapy contains ddC-	Commentary 18

The premise of the above rule is for the inference engine to determine whether or not a therapy being evaluated (i.e., "eval therapy") contains the antiretroviral drug "ddC". If a therapy does contain the antiretroviral drug ddC, the action called for by the conclusion of the rule is to attach "Commentary 18" to the therapy. Commentary 18 may be a piece of text that provides a user with the necessary information about therapies containing ddC.

Exemplary rules which may comprise one or more knowledge bases according to the present invention are listed below in Table 3.

TABLE 3

Therapy initiation/change: Rules that provide information on therapy change or initiation
Boundary condition rules: Limits for values, intervals for values to be updated
Comment Data Aging rules: These rules warn the user that the data in certain fields is getting old and that the most current values in the system will be used.
Rules that filter therapies due to drug interactions in ARV drug combinations
Rules that filter therapies due to medical conditions
Rules that filter therapies due to genotypic mutations in patient's plasma HIV
Rules that filter therapies due to phenotypic sensitivity/resistance
Antiretroviral therapy ranking rules
General dosage rules
Solid dosage rule
Dosage modifications due to ARV-ARV drug combination
Dosage modification due to ARV-NonARV interaction
Dosage modification due to medical condition
Comment determined
General commentary rules
Commentaries added due to medical conditions
Commentaries added due to drug interactions
Commentaries added due to drug combination
Delivery size rules

Using the various knowledge bases and patient information of the present invention (21–25, FIG. 2), the inference engine (26, FIG. 2) can evaluate potential therapy options for a patient based on a patient's medical history (including therapy history) and current laboratory values. Accordingly multiple antiretroviral drug combinations can be quickly and accurately analyzed for a particular patient. Furthermore, the inference engine can quickly provide guidance in the areas listed below in Table 4.

TABLE 4

Data Integrity	Is the patient lab and assessment data getting too old to be considered reliable? Are there conflicts between lab data such as phenotype data which indicates resistance to one or more antiretroviral drugs in the patient's current therapy and current viral load data which indicates significant viral suppression?
Therapy Performance	Should antiretroviral therapy be initiated for the patient? Is the patient's current therapy achieving good initial and long-term viral suppression or should the therapy be changed? Are there potential non-compliance issues as demonstrated by a lack of viral suppression with a regimen when current genotype or phenotype data does provide explanation for the failure by demonstrating resistance to any drugs in the patient current therapy?
Dosage	What are the base and adjusted dosages of antiretroviral drugs in a given therapy? Are there any special specific dosage administration instructions? What are options if patient can only take liquid dosage forms?
Contra-indications	Which antiretroviral drugs can be used with each other and what dosage adjustments are required? Are there any contraindications or interactions between antiretroviral drugs in patient's current therapy or potential therapies and the non-antiretroviral drugs patient is taking and if so what are they and what, if any, dosage adjustments are required?
Medical Conditions	Are there any medical conditions to be aware of in deciding an appropriate therapy for patient? What, if any, effect do current or historical medical conditions have on each therapy option?
Drug Cost and Delivery Data	How much does each therapy option cost? What is the dosing frequency of the drugs in the therapy? What is the pill count and optimum delivery size for the least number of pills?
Therapy Options	What are all the drug combination therapy options for patient? How can physician instantly assess which of the hundreds of potential combinations will be the most effective for patient? What information from the package inserts from each drug apply specifically to patient? What is the relative antiviral efficacy of each therapy? Are there special considerations that might make one therapy more or effective for patient?
Resistance	What drugs are patient's virus current genotypic or phenotypic profile known to be associated with resistance to? Which antiretroviral drugs are more effective against resistant strains when used together? Which drugs (if any) used in historical therapies are most likely to be effective if recycled into a new therapy? Can any of the drugs in patient's current therapy be recycled into the next therapy?

User Interface

Referring now to FIGS. 4–9, exemplary user interfaces according to the present invention will be illustrated. In FIG. 4, a medical history user interface 50 for entering data about a patient's medical history according to the present invention is illustrated. The medical history user interface 50 can be displayed by activating the "Medical History" tab 50*a*. The illustrated medical history user interface 50 allows a

user to create, save, update and print patient records. When a user adds a new patient, the medical history user interface **50** appears with empty data entry fields. Data entry fields for receiving information via a GUI are well known to those of skill in the art and need not be described further herein. When a user opens a patient record for editing, the medical history user interface **50** appears with patient data in the various fields. Preferably color is used to highlight critical or required information in a patient record.

Important elements in the illustrated medical history user interface **50** include a "print" button **51** for printing a patient record and therapeutic treatment regimen details; a "save" button **52** for saving a patient record; and a "speed entry" check box **53** for allowing a user to move quickly between entry fields. In addition, there are multiple group headings **54** that divide a patient's medical history into related categories. Each group contains entry fields in which a user can add patient information. An "add" button **55** allows a user to add new information to a patient record for a selected group. A "delete" button **56** allows a user to delete patient information for a selected group (although the original information is still recorded in the database). A "history" button **57** allows a user to review a patient's historical data for each selected group.

After completing a patient's medical history, an inference engine analyzes the data and suggests whether a therapeutic treatment regimen is indicated; if an existing therapeutic treatment regimen should be continued or changed; and the best drug therapies for the selected patient. Often, more than one drug therapy is presented to the user. These drug therapies are preferably ranked according to expected efficacy, frequency in dosage, pill count, and cost. All of these factors can help the user make a decision about what therapy to use for the selected patient. When a user clicks on a drug therapy in the presented list, information is provided about the dosage regimens. Also, various warnings, such as drug interaction warnings, and notes about each drug, are presented. An appropriate drug therapy can then be selected.

In FIG. **5**, an exemplary user interface chart **60** for monitoring a patient's condition during a particular drug therapy over a period of time is illustrated. The user interface chart **60** can be displayed by activating the "Chart" tab **60*a***. The illustrated user interface chart **60** tracks the CD4 level against viral load. Along the left-hand side of the Y-axis **61** the CD4 count is plotted. Along the right-hand side of the Y-axis **61** the viral load count is plotted. The lines **62** represent the CD4 test and the viral load test as would be understood by those having skill in the art. Drug therapy for a time period is indicated within the area of the chart user interface **60** indicated as **63**. Time is plotted along the X-axis **64**, as illustrated.

In FIG. **6**, a therapy evaluation user interface **70** that facilitates evaluation of various therapy options with respect to relative efficacy, dosage, frequency, cost, medical complications and drug interactions is illustrated. The therapy evaluation user interface **70** can be displayed by activating the "Therapy Evaluation" tab **70*a***. Important elements in the illustrated therapy evaluation user interface **70** include an "Evaluate Current Therapy" button **71** for initiating an evaluation of a current therapy and a "Current Therapy" field **72** that lists a patient's current therapy. Detailed information about a patient's therapy is displayed in the therapy details box **73**. A therapy displayed within box **73** is identified in box **74**.

Multiple check boxes **75** are provided that allow a user to control how information is displayed within the therapy evaluation user interface **70**. Within the therapy list box **76**, a list of available therapies for a patient can be displayed. In the illustrated embodiment the drugs are listed in standard abbreviated form. Other information displayed with each drug may include that listed below in Table 5.

TABLE 5

Efficacy Rating	Lists the therapy according to expected effectiveness only, regardless of patient specific considerations (1 is most effective).
Adjusted Score	This number uses the Efficacy Rating as a base and then the system adjusts it up or down based on patient specific conditions (1 is most effective).
Safety Considerations	A brief two or three word summary of the alerts associated with the therapy.
Frequency	Lists the dosage frequency (q12h, q24h, etc.).
Pills	Lists the total number of pills required per day for the complete regimen.
Cost	Lists the total cost of the regimen per day.
Medical Alert	Displays a Y if there is one or more Yellow Medical Alerts and an R ifthere is one or more Red Medical Alerts associated with the therapy.
Drug Interaction	Displays a Y if there is one or more Yellow Drug Interaction Alerts and an R if there is one or more Red Drug Interaction Alerts associated with the therapy.

A list of available antiretroviral drugs is displayed within box **77**. A user desiring to evaluate a particular combination of drugs can click the appropriate check boxes **77*a*** to review information in the therapy details box **73**. A "Use as Current Therapy" button **78** allows a user to apply a particular therapy to a patient. Various hyperlinks **79** within the therapy details box **73** allow a user to display specific information about a therapy evaluation. For example, a user can be allowed to view a rule which is associated with the displayed text.

Resistance evaluation alerts **80** can be provided adjacent each available antiretroviral drug displayed within box **77**. For example, a blue "G" icon can be used to indicate that a patient's last genotype test contains mutations which are known to be associated with full or partial resistance to the antiretroviral drug. A red "P" icon can be used to indicate that a patient's last phenotype test demonstrates resistance to the antiretroviral drug.

Within the therapy list box **76**, various symbols (described in FIG. **7**) can be utilized to provide information about a drug therapy option. These symbols provide an instant graphical warning level for each therapy option. Some symbols, such as a red exclamation point, indicate that there is critical, possibly life threatening information in the therapy details box **73** for that therapy which must be read in order for that therapy to be properly utilized.

When a drug therapy from the therapy list box **76** is selected by a user for evaluation, the therapy details box **73** of FIG. **6** can be displayed in "full screen" mode as illustrated in FIG. **8**. Important elements in the illustrated therapy details box **73** include an identification box **73*a*** for identifying the therapy being evaluated; a "Use as Current Therapy" button **78** that allows a user to apply a particular therapy to a patient; and a "Show Therapies" button **73*b*** that returns the therapy details box **73** back to half-screen size as illustrated in FIG. **6**. In addition, various hyperlinks may be embedded within text displayed within the therapy details box **73** that can be activated by a user to display various types of information. Eye catching alert banner(s) **73*c*** and text **73*d*** can be displayed at the top of the therapy details box **73** as illustrated. Dosages **73*e*** of each drug, along with

special administration instructions, can be displayed within the therapy details box **73** as illustrated. Dosage adjustment information **73*f*** and various warnings and advisories **73*g*** can also be displayed within the therapy details box **73** as illustrated.

According to a preferred embodiment of the present invention, therapeutic treatment regimens are not displayed to a user if an invalid drug is selected for treatment of a patient.

Physicians Desk Reference®

According to a preferred embodiment of the present invention, the Physicians Desk Reference® (PDR®) **28**, which is a known drug reference source, is fully integrated with the system **20** of FIG. **2**. Users can access the PDR® drug abstracts for antiretroviral drugs listed in the therapy list box **76** of the therapy evaluation user interface **70** of FIG. **6**. In addition, users can access the PDR® on-line Web database to obtain additional information about a specific drug or to research a substitute for a contraindicated drug. When a user selects a drug within the therapy list box **76** of the therapy evaluation user interface **70**, a web browser preferably is launched and the PDR® on-line Web database is accessed. Information can also be extracted from the PDR® on-line Web database to provide drug selection lists for non-antiretroviral drugs that a patient may be taking and to define relationships between brand name and generic drugs.

As illustrated in FIG. **9**, a PDR® pop-up menu **90** may be provided that can be activated from within the therapy list box **76** of the therapy evaluation user interface **70** of FIG. **6**. From the PDR® pop-up menu **90** a user can access various information from the PDR® including, but not limited to, drug abstracts, and generic components contained within a brand name drug.

The following non-limiting examples illustrate various aspects of the present invention. These examples are provided for illustrative purposes only, and are not intended to be limiting of the invention.

EXAMPLE 1

Example 1 will be explained with reference to FIGS. **10A–10D**. Referring to FIG. **10A**, a medical history user interface **50** containing evaluated data for patient "demol" is illustrated. The group heading "Hemoglobin" **54*a*** has changed colors to indicate to a user that the patient has an abnormally low hemoglobin value from a previous (historical) blood sampling. When the therapy evaluation tab **70*a*** is activated to display the therapy evaluation user interface **70** (FIG. **10B**) the associated medical condition warning of a history of anemia and the caution notification if using drugs known to be associated with hematopoetic toxicity is triggered as illustrated in the therapy details box **73** of FIG. **10B**.

In addition, the group heading "Renal Function" **54*b*** in FIG. **10A** has changed colors to warn a user of potential renal dysfunction and is also indicated by the low estimated creatinine clearance rate in field **F1** (which the system calculates using a mathematical formula taking patient age, sex, weight, and serum creatinine values—all of which are fields of the "Medical History" user interface **50**). This information is pointed out to the user and is used if dosage adjustments are required for drugs that are known to be affected (cleared) by renal function.

Current and the next most recent $CD4^+$ cell count and viral load are displayed (**F2**, medical history user interface **50**). This information is also used to determine when to start or change therapy and to evaluate the initial antiviral efficacy of a newly administered antiviral regimen.

Current and historical values for all fields in the medical history user interface **50** (FIG. **10A**) can be viewed by pressing the "H" button beside fields that have this button.

In FIG. **10C**, the "Chart" user interface **60** has been activated. HIV RNA (viral load) is plotted on a log scale, the CD4 count is plotted on a linear scale, and the drug treatments are shown as Gantt bars on the horizontal date scale at the bottom of the chart user interface **60**.

In FIG. **10D**, the "Change Therapy Recommendation" message box **MB1** pops up when the "Therapy Evaluation" tab **70*a*** is selected. This box represents the processing of the data from the "Medical History" tab and the knowledge base output, including objective rules derived from published treatment guidelines, indicating that initiation of therapy, or a change of therapy in this case, may be called for if the other variable(s) indicated in the message have been addressed.

The list of available therapies and associated ranking order may be shown within the therapy details box **73** of FIG. **10B**. This represents the output of the knowledge base for therapy selection. Included with the list of therapies can be any of the following: safety advisories (dosage adjustment, drug interaction, etc.) with a yellow triangle or red exclamation warning symbols; number of pills; daily cost of all three drugs; dosing regimen (q 8 h, q 12 h, etc.); and dosages for all drugs in a regimen (including dosage adjustments if necessary) and pertinent information specific to the patient is listed in the dialog box.

EXAMPLE 2

Example 2 will be explained with reference to FIGS. **11A–11E**, and relates to patient file "ARV naive1" which is an example of an HIV-infected patient who has not been treated with anti-HIV drugs previously. In FIG. **11A**, a medical history user interface **50** containing evaluated data for patient "ARV naive1" is illustrated. In FIG. **11B**, when the "Therapy Evaluation" tab **70*a*** is activated to display the therapy evaluation user interface **70**, a "Boundary and Prequalification Messages" message box **MB2** pops up indicating that according to the current, published, HIV treatment guidelines, the patient should be initiated on antiviral therapy and that the current guidelines recommend combinational therapy.

In FIG. **11C**, the therapy evaluation user interface **70** has been activated and demonstrates features/functions associated with therapy evaluation including a general warning **W1** and advisories **A1**, **A2**, and **A3** for the patient related to treatment of the disease (e.g., whether therapy should be initiated or changed) or related to a specific therapy selected from the list box which is being evaluated by the user.

FIG. **11D** illustrates various information that is displayable by clicking on an individual therapy in the therapy list box **76** of FIG. **11C**. Information displayed includes dosages of all drugs with general and patient-specific warnings and advisories.

The features available by right clicking on any therapy listed in the therapy list box **76** of FIG. **11C** are illustrated in FIG. **11E** and include: linking to an electronic PDR® to show drug package insert information or perform drug search information; showing or hiding columns of information displayed within the therapy list box; linking to a publication or abstract associated with a therapy that has a "book" icon associated therewith; and various printing functions.

EXAMPLE 3

Example 3 will be explained with reference to FIGS. 12A–12C, and relates to patient file "Features1" which illustrates some important functions/features that a system according to the present invention can provide for highly drug experienced patients who may have developed resistance associated with the use of several antiviral drugs. Features, including functions attributed to the new resistance and historical therapy rules are illustrated and includes:

1) Potential drug resistance advisories (A1, FIG. 12A) when the chart tab 60*a* is activated, or (A2, FIG. 12B) when the therapy evaluation tab 70*a* is activated;
2) The heads up "P" and "G" indicators (I1 and I2, FIG. 12B) to remind of phenotypic or genotypic resistance associated with certain anti-HIV compounds as demonstrated for this patient (including indication of expected/anticipated genotypic resistance, as a result of cross-resistance, to a drug that a patient may not be taking currently or has not previously taken);
3) The drug interaction warning system (indicated by warning W3, FIG. 12C). Warning W3 is for the interaction between Nevirapine and rifabutin (which was selected from the list of non-antiretroviral drugs available as part of the medical history user interface 50). The drug interaction warning message may be viewed from the medical history user interface 50 by "right-clicking" the non-ARV title bar 54C, which has turned yellow indicating the presence of an ARV-nonARV drug interaction. This information is also prominently displayed for the user on the therapy evaluation user interface 70 as a text message (W3, FIG. 12B) as well as in the "Safety Considerations" section of the drug list box (76, FIG. 12B); and
4) The chart user interface 60 (FIG. 12A) illustrates the viral load, CD4, drug therapies, and associated drug resistance in graphic form for the user to evaluate.

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined in the claims. Therefore, it is to be understood that the foregoing is illustrative of the present invention and is not to be construed as limited to the specific embodiments disclosed, and that modifications to the disclosed embodiments, as well as other embodiments, are intended to be included within the scope of the appended claims. The invention is defined by the following claims, with equivalents of the claims to be included therein.

That which is claimed is:

1. A method for guiding the selection of a therapeutic treatment regimen for a patient with a chronic known disease or medical condition, said method comprising:

(a) providing patient information to a computing device, said patient information including prior therapeutic treatment regimen information for said chronic known disease or medical condition, said computer device comprising:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) generating in said computing device from said patient information and said first knowledge base a listing of available therapeutic treatment regimens for said patient; and

(c) generating in said computing device advisory information for one or more therapeutic treatment regimens for said patient in said listing based on said patient information and said expert rules.

2. A method according to claim 1, further comprising the steps of:

(d) entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not included in said first knowledge base;

(e) generating in said computing device advisory information for said user-defined combination therapeutic treatment regimen.

3. A method according to claim 1, further comprising the steps of:

(f) entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said listing; and

(g) generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

4. A method according to claim 1, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

5. A method according to claim 1, wherein said listing of available therapeutic treatment regimens for said patient comprises a ranked listing of available therapeutic treatment regimens for said patient.

6. A method according to claim 1, wherein said patient information includes prior patient information stored in said computing device.

7. A method according to claim 1, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

8. A method according to claim 1, wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

9. A method according to claim 7, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

10. A method according to claims 7, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

11. A method according to claim 7, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

12. A method according to claim 1, wherein said known disease or medical condition is one where multiple prophylactic or therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease.

13. A method according to claim 1, wherein said known disease or medical condition is a cardiovascular disease.

14. A method according to claim 1, wherein said known disease or medical condition is a pulmonary disease.

15. A method according to claim 1, wherein said known disease or medical condition is a neurologic disease.

16. A method according to claim 1, wherein said known disease or medical condition is cancer.

17. A method according to claim 1, wherein said known disease or medical condition is a urinary tract infection.

18. A method according to claim 1, wherein said known disease or medical condition is hepatitis.

19. A method according to claim 1, wherein said known disease or medical condition is HIV-1 infection.

20. A method according to claim 1, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

21. A method according to claim 1, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

22. A method according to claim 1, further comprising the step of:

(d) accessing, via said computing device, information for one or more therapeutic treatment regimens from a drug reference source.

23. A system for guiding the selection of a therapeutic treatment regimen for a patient with a chronic known disease or medical condition, said system comprising:

(a) a computing device comprising:
  - a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;
  - a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for said disease or medical condition;
  - a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) means for providing patient information to said computing device, said patient information including prior therapeutic treatment regimen information for said chronic known disease or medical condition;

(c) means for generating in said computing device from said patient information and said first knowledge base a listing of therapeutic treatment regimens for said patient for said chronic known disease or medical condition; and

(d) means for generating in said computing device advisory information for one or more therapeutic treatment regimens for said patient in said listing based on said patient information and said expert rules.

24. A system according to claim 23, further comprising:

(e) means for entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not generated or displayed via said first knowledge base;

(f) means for generating in said computing device advisory information for said user-defined combination therapeutic treatment regimen.

25. A system according to claim 23, further comprising:

(f) means for entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said listing; and

(g) means for generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

26. A system according to claim 23, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

27. A system according to claim 23, wherein said listing of available therapeutic treatment regimens for said patient comprises a ranked listing of available therapeutic treatment regimens for said patient.

28. A system according to claim 23, wherein said patient information includes prior patient information stored in said computing device.

29. A system according to claim 23, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

30. A system according to claim 23, wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

31. A system according to claim 29, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

32. A system according to claim 29, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

33. A system according to claim 29, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

34. A system according to claim 23, wherein said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease or medical condition.

35. A system according to claim 23, wherein said known disease or medical condition is a cardiovascular disease.

36. A system according to claim 23, wherein said known disease or medical condition is a pulmonary disease.

37. A system according to claim 23, wherein said known disease or medical condition is a neurologic disease.

38. A system according to claim 23, wherein said known disease or medical condition is cancer.

39. A system according to claim 23, wherein said known disease or medical condition is a urinary tract infection.

40. A system according to claim 23, wherein said known disease or medical condition is hepatitis.

41. A system according to claim 23, wherein said known disease or medical condition is HIV-1 infection.

42. A system according to claim 23, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

43. A system according to claim 23, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

44. A system according to claim further comprising:

(e) means for accessing, via said computing device, information for one or more therapeutic treatment regimens from a standard drug reference source.

45. A computer program product for guiding the selection of a therapeutic treatment regimen for a patient with a chronic known disease or medical condition, said computer program product comprising a computer usable storage medium having computer readable program code means embodied in the medium, the computer readable program code means comprising:

(a) computer readable program code means for generating:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

(b) computer readable program code means for providing patient information, said patient information including prior therapeutic treatment regimen information for said chronic known disease or medical condition;

(c) computer readable program code means for generating from said patient information and said first knowledge base a listing of available therapeutic treatment regimens for said patient for said chronic known disease or medical condition; and

(d) computer readable program code means for generating advisory information for one or more therapeutic treatment regimens for said patient in said listing based on said patient information and said expert rules.

46. A computer program product according to claim 45, further comprising:

(e) computer readable program code means for entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not generated or displayed via said first knowledge base;

(f) computer readable program code means for generating advisory information for said user-defined combination therapeutic treatment regimen.

47. A computer program product according to claim 46, further comprising:

(g) computer readable program code means for entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommnended from said listing; and

(h) computer readable program code means for generating advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

48. A computer program product according to claim 45, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information.

49. A computer program product according to claim 45, wherein said patient information includes prior patient information.

50. A computer program product according to claim 45, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

51. A computer program product according to claim 45 wherein said computer readable program code means comprises computer readable program code means for generating a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

52. A computer program product according to claim 50, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

53. A computer program product according to claim 50, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

54. A computer program product according to claim 50, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

55. A computer program product according to claim 45, wherein said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease or medical condition.

56. A computer program product according to claim 45, wherein said known disease or medical condition is a cardiovascular disease.

57. A computer program product according to claim 45, wherein said known disease or medical condition is a pulmonary disease.

58. A computer program product according to claim 45, wherein said known disease or medical condition is a neurologic disease.

59. A computer program product according to claim 45, wherein said known disease or medical condition is cancer.

60. A computer program product according to claim 45, wherein said known disease or medical condition is a urinary tract infection.

61. A computer program product according to claim 45, wherein said known disease or medical condition is hepatitis.

62. A computer program product according to claim 45, wherein said known disease or medical condition is HIV-1 infection.

63. A computer program product according to claim 45, wherein said first knowledge base comprises a plurality of different combination therapeutic treatment regimens.

64. A computer program product according to claim 45, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

65. A computer program product according to claim 45, further comprising:

(e) computer readable program code means for accessing information for one or more therapeutic treatment regimens from a standard drug reference source.

66. A computer program product according to claim 45, wherein said listing of available therapeutic treatment regimens for said patient is a ranked listing of available therapeutic treatment regimens for said patient.

* * * * *

CERTIFICATE OF SERVICE

I hereby certify that on June 20, 2013, I electronically filed the foregoing documents:

APPELLANTS' OPENING BRIEF

with the Clerk for the Court using the CM/ECF system, which will then send a notification of such filing (NEF) to the following:

Counsel for Plaintiff SmartGene, Inc.

Maurice U. Cahn
Frederick N. Samuels
Cahn & Samuels, LLP
1100 17th St., NW
Suite 401
Washington, DC 20036
Tel: 202-331-8777
Fax: 202-331-3838
Email: maurice.cahn@cahnsamuels.com
Email: frederick.samuels@samuels.com

/s/ Robert R. Sachs
Robert R. Sachs

Counsel for Appellants
Advanced Biological Laboratories, SA and
ABL Patent Licensing Technologies, SARL

CERTIFICATE OF COMPLIANCE WITH RULE 32(A)

This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B). The brief contains 13,714 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). The brief has been prepared in a proportionally spaced typeface using Microsoft Word 2007 in 14-point Times New Roman font.

Dated: June 20, 2013

/s/ Robert R. Sachs

Counsel for Appellants
Advanced Biological Laboratories, SA and
ABL Patent Licensing Technologies, SARL